SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: P. Spivack Examiner #: 70400 Date: 10/1/03
Art Unit: 1614 Phone Number 30 8 4703 Serial Number: 10/087596
Mail Box and Bldg/Room Location: 2D01 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Compositions for Management of Serotonin-Mediated Disorders

Inventors (please provide full names): Mark Eutrie
Tom Jerussi P Rupin C Senanayake

Earliest Priority Filing Date: 3/2/01

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search

A pharmaceutical preparation comprising a nefazodonoid and a serotonin reuptake inhibitor (SRI), in a pharmaceutically acceptable excipient.

wherein the nefazodonoid is selected from nefazodone, hydroxynefazodone, oxonefazodone, a mixture thereof, and pharmaceutically acceptable salts thereof.

elected = SSRI = fluoxetine prozac

Please include inventors search.

Thanks

****

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher:	NA Sequence (#)	STN
Searcher Phone #:	AA Sequence (#)	Dialog
Searcher Location:	Structure (#)	Questel/Orbit
Date Searcher Picked Up:	Bibliographic	Dr.Link
Date Completed:	Litigation	Lexis/Nexis

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=> fil reg; d stat que l8; d stat que l10; d stat que l14; d stat que l16
FILE 'REGISTRY' ENTERED AT 16:39:42 ON 03 OCT 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    1 OCT 2003  HIGHEST RN 596788-60-2
DICTIONARY FILE UPDATES:   1 OCT 2003  HIGHEST RN 596788-60-2

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

L3                STR
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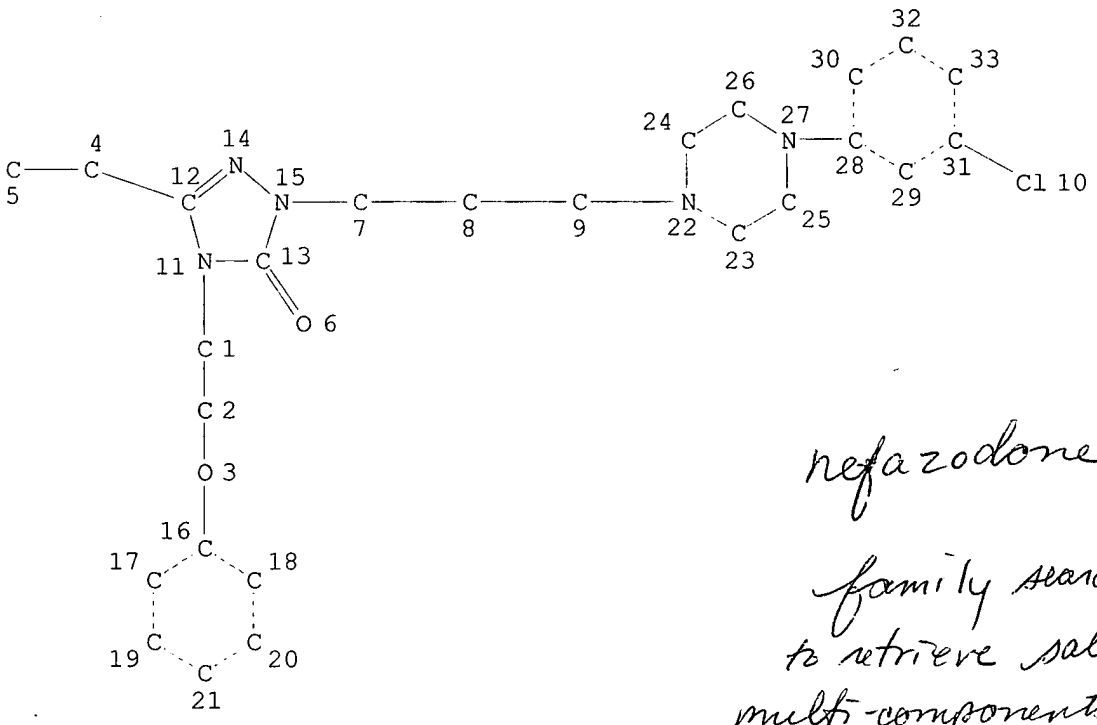

nefazodone

family search done to retrieve salts, stereoisomers, multi-component substances, & radiolabelled forms.

```
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  33

STEREO ATTRIBUTES: NONE
L8            11 SEA FILE=REGISTRY FAM FUL L3
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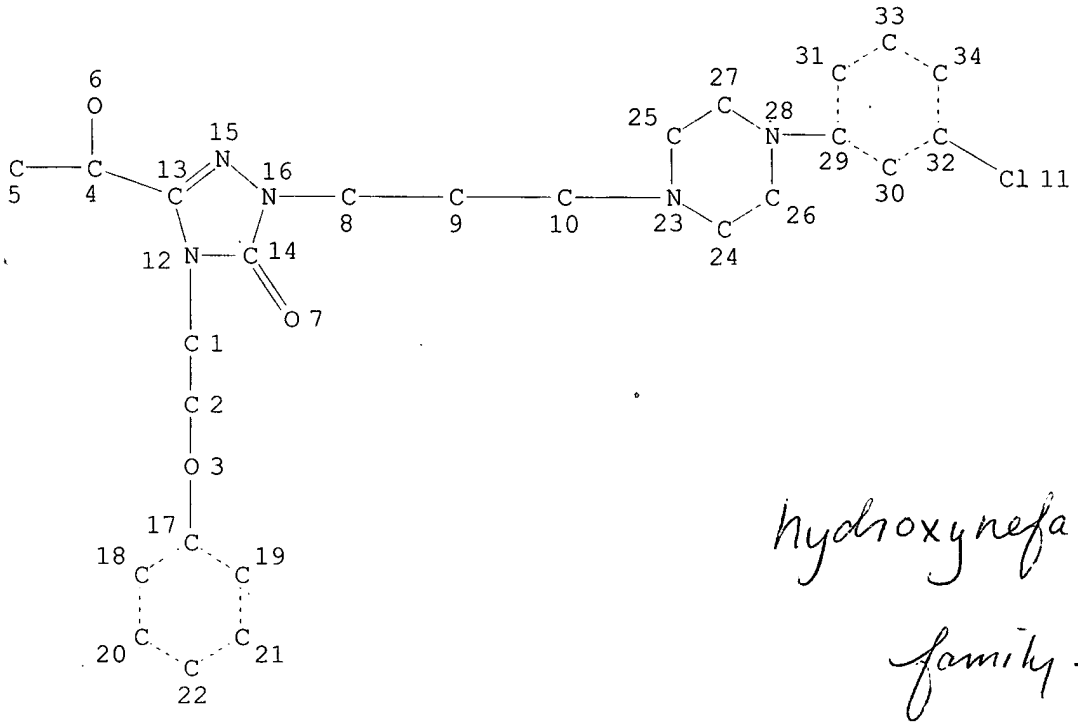
100.0% PROCESSED 64 ITERATIONS 11 ANSWERS
SEARCH TIME: 00.00.01

L4 STR



hydroxynefazodone

family search

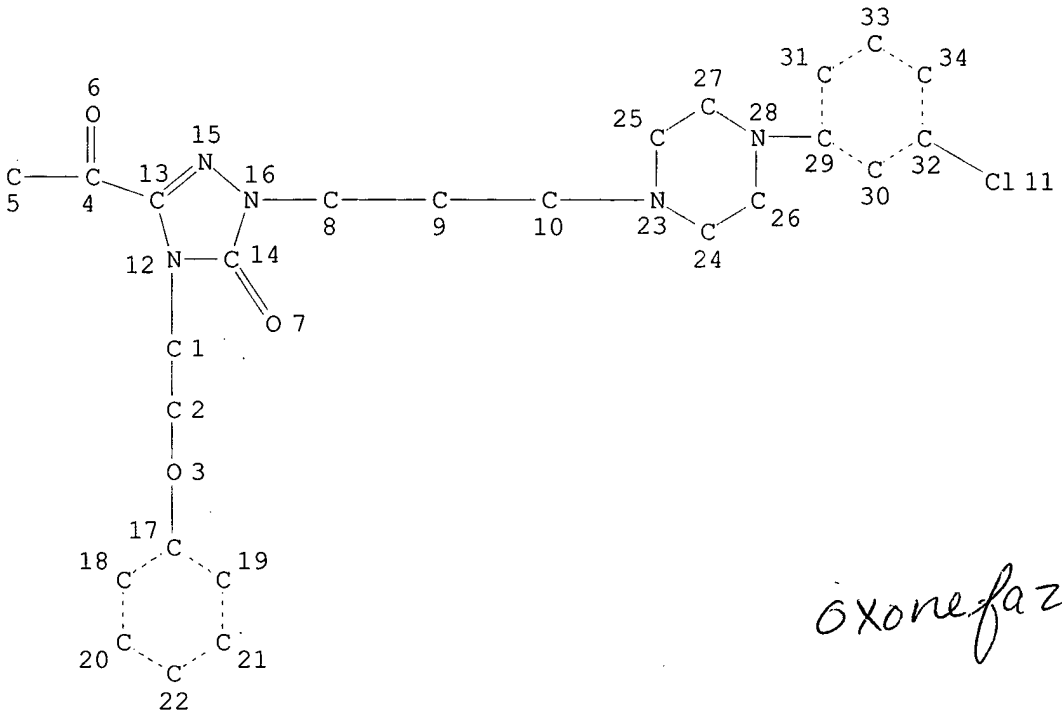
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 34

STEREO ATTRIBUTES: NONE
L10 7 SEA FILE=REGISTRY FAM FUL L4

100.0% PROCESSED 18 ITERATIONS 7 ANSWERS
SEARCH TIME: 00.00.01

L12 STR



oxonefazodone

family search

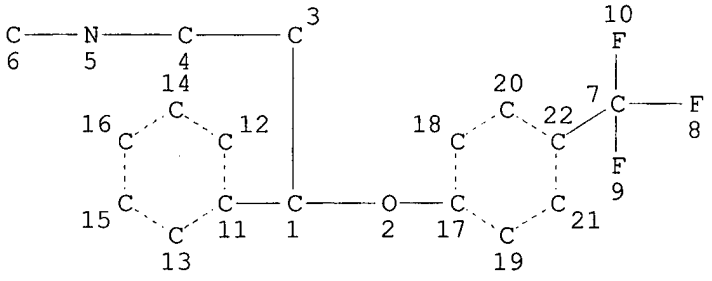
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 34

STEREO ATTRIBUTES: NONE
L14 2 SEA FILE=REGISTRY FAM FUL L12

100.0% PROCESSED 18 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

L6 STR



fluoxetine

family search

NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
L16 53 SEA FILE=REGISTRY FAM FUL L6

100.0% PROCESSED 256 ITERATIONS 53 ANSWERS
SEARCH TIME: 00.00.01

=> fil capl; d que nos l26; d que nos l27; s l26 or l27

FILE 'CAPLUS' ENTERED AT 16:39:43 ON 03 OCT 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Inventor search

FILE COVERS 1907 - 3 Oct 2003 VOL 139 ISS 15
FILE LAST UPDATED: 2 Oct 2003 (20031002/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

L22 264 SEA FILE=CAPLUS ABB=ON CURRIE M?/AU
L23 59 SEA FILE=CAPLUS ABB=ON JERUSSI T?/AU
L24 299 SEA FILE=CAPLUS ABB=ON RUBIN P?/AU
L25 150 SEA FILE=CAPLUS ABB=ON SENANAYAKE C?/AU
L26 1 SEA FILE=CAPLUS ABB=ON L22 AND L23 AND L24 AND L25

L3 STR
L4 STR
L6 STR
L8 11 SEA FILE=REGISTRY FAM FUL L3
L10 7 SEA FILE=REGISTRY FAM FUL L4
L12 STR
L14 2 SEA FILE=REGISTRY FAM FUL L12
L16 53 SEA FILE=REGISTRY FAM FUL L6
L17 346 SEA FILE=CAPLUS ABB=ON L8 OR NEFAZODONE/OBI
L18 36 SEA FILE=CAPLUS ABB=ON L10 OR HYDROXYNEFAZODONE/OBI
L19 2 SEA FILE=CAPLUS ABB=ON L14 OR OXONEFAZODONE/OBI
L20 2952 SEA FILE=CAPLUS ABB=ON L16 OR FLUOXETINE/OBI
L21 130 SEA FILE=CAPLUS ABB=ON (L17 OR L18 OR L19) AND L20
L22 264 SEA FILE=CAPLUS ABB=ON CURRIE M?/AU
L23 59 SEA FILE=CAPLUS ABB=ON JERUSSI T?/AU
L24 299 SEA FILE=CAPLUS ABB=ON RUBIN P?/AU
L25 150 SEA FILE=CAPLUS ABB=ON SENANAYAKE C?/AU
L27 2 SEA FILE=CAPLUS ABB=ON (L22 OR L23 OR L24 OR L25) AND L21

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L145          2 L26 OR L27

=> fil medl; d que nos 160; fil embase; d que nos l75

FILE 'MEDLINE' ENTERED AT 16:39:47 ON 03 OCT 2003

 FILE LAST UPDATED: 2 OCT 2003 (20031002/UP). FILE COVERS 1958 TO DATE.

 On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L50         193 SEA FILE=MEDLINE ABB=ON  CURRIE M?/AU
L51          35 SEA FILE=MEDLINE ABB=ON  JERUSSI T?/AU
L52         767 SEA FILE=MEDLINE ABB=ON  RUBIN P?/AU
L53           6 SEA FILE=MEDLINE ABB=ON  SENANAYAKE C?/AU
L55        4299 SEA FILE=MEDLINE ABB=ON  FLUOXETINE/CT
L56         355 SEA FILE=MEDLINE ABB=ON  NEFAZODONE/CN
L57          14 SEA FILE=MEDLINE ABB=ON  HYDROXYNEFAZODONE/CN
L60           0 SEA FILE=MEDLINE ABB=ON  (L50 OR L51 OR L52 OR L53) AND (L55
                 OR L56 OR L57)


FILE 'EMBASE' ENTERED AT 16:39:47 ON 03 OCT 2003
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 FILE COVERS 1974 TO 2 Oct 2003 (20031002/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L66          43 SEA FILE=EMBASE ABB=ON  SENANAYAKE C?/AU
L67         682 SEA FILE=EMBASE ABB=ON  RUBIN P?/AU
L68          37 SEA FILE=EMBASE ABB=ON  JERUSSI T?/AU
L69         181 SEA FILE=EMBASE ABB=ON  CURRIE M?/AU
L70       14776 SEA FILE=EMBASE ABB=ON  FLUOXETINE/CT
L71        2077 SEA FILE=EMBASE ABB=ON  NEFAZODONE/CT
L72          33 SEA FILE=EMBASE ABB=ON  HYDROXYNEFAZODONE/CT
L75           2 SEA FILE=EMBASE ABB=ON  (L66 OR L67 OR L68 OR L69) AND (L70 OR
                 L71 OR L72)

=> fil drugu; d que nos l126

FILE 'DRUGU' ENTERED AT 16:39:47 ON 03 OCT 2003
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FILE LAST UPDATED: 2 OCT 2003       <20031002/UP>
>>>  DERWENT DRUG FILE (SUBSCRIBER)  <<<
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>>>  SDI'S MAY BE RUN WEEKLY OR MONTHLY AS OF JUNE 2001.  <<<
>>>  (WEEKLY IS THE DEFAULT). FOR PRICING INFORMATION     <<<
>>>  SEE HELP COST                                        <<<

>>>  FILE COVERS 1983 TO DATE  <<<
>>>  THESAURUS AVAILABLE IN /CT  <<<



L117         157 SEA FILE=DRUGU ABB=ON  RUBIN P?/AU
L118          22 SEA FILE=DRUGU ABB=ON  SENANAYAKE C?/AU
L119          53 SEA FILE=DRUGU ABB=ON  CURRIE M?/AU
L120          19 SEA FILE=DRUGU ABB=ON  JERUSSI T?/AU
L122        5746 SEA FILE=DRUGU ABB=ON  FLUOXETINE/CT
L123         703 SEA FILE=DRUGU ABB=ON  NEFAZODONE/CT
L124          52 SEA FILE=DRUGU ABB=ON  HYDROXYNEFAZODONE/CT
L126           1 SEA FILE=DRUGU ABB=ON  (L117 OR L118 OR L119 OR L120) AND
                 (L122 OR L123 OR L124)


=> dup rem l126,l145,l75
FILE 'DRUGU' ENTERED AT 16:40:18 ON 03 OCT 2003
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FILE 'CAPLUS' ENTERED AT 16:40:18 ON 03 OCT 2003
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PROCESSING COMPLETED FOR L126
PROCESSING COMPLETED FOR L145
PROCESSING COMPLETED FOR L75
L146           4 DUP REM L126 L145 L75 (1 DUPLICATE REMOVED)
                 ANSWER '1' FROM FILE DRUGU
                 ANSWERS '2-3' FROM FILE CAPLUS
                 ANSWER '4' FROM FILE EMBASE

=> d iall 1; d ibib ab hitrn 2-3; d iall 4

L146  ANSWER 1 OF 4  DRUGU  COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 1
ACCESSION NUMBER: 2001-47999  DRUGU   C
TITLE:            A practical asymmetric synthesis of (R)-fluoxetine and its
                  major metabolite (R)-norfluoxetine.
AUTHOR:           Hilborn J W; Lu Z H; Jurgens A R; Fang Q K; Byers P; Wald S
                  A; Senanayake C H
CORPORATE SOURCE: Sepracor
LOCATION:         Marlborough, Mass., USA; Windsor, N.S., Can.
SOURCE:           Tetrahedron Lett. (42, No. 51, 8919-21, 2001) 27 Ref.
                  CODEN: TELEAY       ISSN:  0040-4039
AVAIL. OF DOC.:   Sepracor, Inc., Chemical Process R&D, 111 Locke Drive,
                  Marlborough, MA 01752, U.S.A. (Z.H.L.) (e-mail:
                  zlu@sepracor.com).
LANGUAGE:         English
DOCUMENT TYPE:    Journal

ABSTRACT:

A simple, chromatography-free process is described for the asymmetric synthesis
of (R)-fluoxetine and (R)-norfluoxetine tartrate via the optically pure cyclic
carbamate (5). The synthesis involved CBS reduction and Hofman rearrangement.
The procedure used low-cost raw materials and conventional reagents, giving the
```

(R)-enantiomers of fluoxetine and norfluoxetine tartrate with chemical purity and ee better than 99%.

SECTION HEADING: C Chemistry

CLASSIF. CODE: 32 Psychotropic
71 Medicinal Chemistry

CONTROLLED TERM:
TOTAL *FT; SYNTH. *FT; STEREOISOMER *FT; METABOLITE *FT; STEREOCHEM. *FT
[01] **FLUOXETINE** *OC; FLUOXETIN *RN; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; OC *FT
CAS REGISTRY NO.: 54910-89-3
[02] NORFLUOXETINE *OC; TARTRATE *OC; NORFLUOXE *RN; BIOSYNTH. *FT; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; OC *FT
CAS REGISTRY NO.: 83891-03-6
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L146 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:695766 CAPLUS
DOCUMENT NUMBER: 137:237719
TITLE: **Hydroxynefazodone** compositions for the management of serotonin-mediated disorders
INVENTOR(S): **Currie, Marc G.; Senanayake, Chris H.; Jerussi, Thomas P.; Rubin, Paul**
PATENT ASSIGNEE(S): Sepracor Inc., USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

parent

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002069951	A2	20020912	WO 2002-US6204	20020301
WO 2002069951	A3	20030306		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003083338	A1	20030501	US 2002-87596	20020301

PRIORITY APPLN. INFO.: US 2001-273113P P 20010302
US 2001-306939P P 20010720
OTHER SOURCE(S): MARPAT 137:237719

AB The present invention provides methods and compns. for conjoint administration of a nefazodonoid and a fluoxetinoid for the treatment of depression and other neurol. conditions. Thus, tablets were prepd. from the following compn.: (S)-hydroxynefazodone 200, clozapine 50, pregelatinized starch 190, microcryst. cellulose 25, Povidone 15, Croscarmellose 10, Mg stearate 3.75, and FD&C Yellow # Lake 2.5 mg, water 5 mL. (S)-hydroxynefazodone was prepd. in a series of steps. The compd.

showed strong affinity for the dopamine D2 receptor.

IT **301530-56-3P 301530-79-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**hydroxynefazodone** compns. for management of serotonin-mediated disorders)

IT **83366-66-9, Nefazodone 98159-82-1**
153707-86-9, Oxonefazodone 301530-51-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**hydroxynefazodone** compns. for management of serotonin-mediated disorders)

IT **301530-74-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(**hydroxynefazodone** compns. for management of serotonin-mediated disorders)

IT **54910-89-3, Fluoxetine 100568-03-4**, (R)-**Fluoxetine**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**hydroxynefazodone** compns. for management of serotonin-mediated disorders)

L146 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:144724 CAPLUS
DOCUMENT NUMBER: 132:185455
TITLE: Oral compositions containing optically pure S-(+)-vigabatrin for prevention or treatment of symptoms of peripheral neuropathy
INVENTOR(S): **Rubin, Paul D.**; Barberich, Timothy J.; Yelle, William E.
PATENT ASSIGNEE(S): Sepracor Inc., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000010554	A2	20000302	WO 1999-US19346	19990824
WO 2000010554	A3	20001130		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2341400	AA	20000302	CA 1999-2341400	19990824
AU 9957844	A1	20000314	AU 1999-57844	19990824
EP 1107748	A2	20010620	EP 1999-945177	19990824
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003520189	T2	20030702	JP 2000-565876	19990824

PRIORITY APPLN. INFO.:
US 1998-97786P P 19980825
US 1998-114456P P 19981230
WO 1999-US19346 W 19990824

AB Compns. for the prevention, treatment, and/or management of the symptoms of peripheral neuropathy and related disorders, drug or alc. addiction or symptoms assocd. with drug or alc. withdrawal involve the use of optically pure S-(+)-vigabatrin (I) or a pharmaceutically acceptable salt. Thus, compressed tablets contained I 10.0, lactose 57.0, starch 20.0, microcryst. cellulose 10.0, hydrogenated vegetable oil 1.5, and PVP 1.5%.

IT **54910-89-3, Fluoxetine 83366-66-9, Nefazodone**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral compns. contg. S-(+)-vigabatrin for prevention or treatment of symptoms of peripheral neuropathy)

L146 ANSWER 4 OF 4 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2002021297 EMBASE
TITLE: Pharmaceutical advertising as a consumer empowerment device.
AUTHOR: **Rubin P.H.**
CORPORATE SOURCE: P.H. Rubin, Department of Economics, Sch. of Law at Emory University, Atlanta, GA, United States
SOURCE: Journal of Biolaw and Business, (2001) 4/4 (59-65).
ISSN: 1095-5127 CODEN: JBBUF8
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Pharmaceutical companies have greatly increased their level of "direct-to-consumer" (DTC) advertising in recent years. For 1998, estimates are that over $1.1 billion was spent on this form of advertising, increased from $850 million in 1997 and $600 million in 1996. In 1998, 84 separate drugs were advertised to consumers. The impetus was a decision in August of 1997 by the Food and Drug Administration to reduce the restrictions on DTC advertising on television. As a result, such ads have become very common on TV, and 32 products were advertised on TV in 1998. Pharmaceutical companies advertise because they think that advertising will make money for them. But how will this make money? It will make money by providing consumers with the information they need to make proper decisions about medication. That is, DTC advertising is profitable exactly because it empowers consumers and enables them to purchase useful drugs. The goals of advertising companies and consumers are both for consumers to have information about the most beneficial drug for particular conditions, and so advertising is beneficial both to manufacturers and to consumers. This article describes emerging trends in DTC within the context of the life sciences sector.

CONTROLLED TERM: Medical Descriptors:
*advertizing
*drug marketing
consumer
drug industry
food and drug administration
television
drug information
decision making
biomedicine
drug cost

Internet
health maintenance organization
drug induced disease: SI, side effect
human
review
Drug Descriptors:
finasteride: PE, pharmacoeconomics
terbinafine: PE, pharmacoeconomics
fluoxetine: PE, pharmacoeconomics
donepezil: PE, pharmacoeconomics
conjugated estrogen plus medroxyprogesterone acetate: PE, pharmacoeconomics
carprofen: PE, pharmacoeconomics
tolterodine: PE, pharmacoeconomics
cetirizine: PE, pharmacoeconomics
etanercept: PE, pharmacoeconomics
hyaluronic acid: PE, pharmacoeconomics
hepatitis B vaccine: PE, pharmacoeconomics
conjugated estrogen: PE, pharmacoeconomics
estradiol: PE, pharmacoeconomics
tamoxifen citrate: PE, pharmacoeconomics
pravastatin: PE, pharmacoeconomics
simvastatin: PE, pharmacoeconomics
atorvastatin: PE, pharmacoeconomics
antihypertensive agent: AE, adverse drug reaction
antihypertensive agent: PE, pharmacoeconomics
oxaprozin: PE, pharmacoeconomics
medroxyprogesterone acetate: PE, pharmacoeconomics
oxybutynin: PE, pharmacoeconomics
estradiol plus norethisterone acetate: PE, pharmacoeconomics
omeprazole: PE, pharmacoeconomics
azithromycin: PE, pharmacoeconomics
sildenafil: PE, pharmacoeconomics
minoxidil: PE, pharmacoeconomics
amfebutamone: PE, pharmacoeconomics
retinoic acid: PE, pharmacoeconomics
ethinylestradiol plus norgestimate: PE, pharmacoeconomics
unindexed drug

CAS REGISTRY NO.: (finasteride) 98319-26-7; (terbinafine) 91161-71-6; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (donepezil) 120011-70-3, 120014-06-4, 142057-77-0; (carprofen) 52263-47-5, 53716-49-7; (tolterodine) 124937-51-5; (cetirizine) 83881-51-0, 83881-52-1; (etanercept) 185243-69-0, 200013-86-1; (hyaluronic acid) 31799-91-4, 9004-61-9, 9067-32-7; (estradiol) 50-28-2; (tamoxifen citrate) 54965-24-1; (pravastatin) 81131-74-0; (simvastatin) 79902-63-9; (atorvastatin) 134523-00-5, 134523-03-8; (oxaprozin) 21256-18-8; (medroxyprogesterone acetate) 71-58-9; (oxybutynin) 1508-65-2, 5633-20-5; (omeprazole) 73590-58-6, 95510-70-6; (azithromycin) 83905-01-5; (sildenafil) 139755-83-2; (minoxidil) 38304-91-5; (amfebutamone) 31677-93-7, 34911-55-2; (retinoic acid) 302-79-4; (ethinylestradiol plus norgestimate) 79871-54-8

CHEMICAL NAME: (1) Proscar; (2) Lamisil; (3) Prozac; (4) Aricept; (5) Aricept; (6) Prempro; (7) Detrol; (8) Premarin; (9) Estraderm; (10) Nolvadex; (11) Daypro; (12) Ditropan; (13) Combipatch; (14) Prilosec; (15) Zithromax; (16) Zyban; (17) Renova; (18) Tricyclen; Rimadyl; Zyrtec; Enbrel; Synvisc; Pravachol; Zocor; Lipitor; Depo provera; Viagra; Propecia; Rogaine

COMPANY NAME: (1) Merck; (2) Sandoz; (3) Lilly; (4) Eisai; (7) Pharmacia

Upjohn; (8) Wyeth Ayerst; (9) Ciba Geigy; (10) Zeneca roche; (11) Searle; (12) Alza; (13) Rhone Poulenc Rorer; (14) Astra Zeneca; (15) Pfizer; (16) Glaxo; (18) Ortho

```
=> fil capl; d que nos l143
FILE 'CAPLUS' ENTERED AT 16:41:30 ON 03 OCT 2003
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FILE COVERS 1907 - 3 Oct 2003  VOL 139 ISS 15
FILE LAST UPDATED: 2 Oct 2003  (20031002/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.
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text search

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L3              STR
L4              STR
L6              STR
L8           11 SEA FILE=REGISTRY FAM FUL L3
L10           7 SEA FILE=REGISTRY FAM FUL L4
L12             STR
L14           2 SEA FILE=REGISTRY FAM FUL L12
L16          53 SEA FILE=REGISTRY FAM FUL L6
L17         346 SEA FILE=CAPLUS ABB=ON  L8 OR NEFAZODONE/OBI
L18          36 SEA FILE=CAPLUS ABB=ON  L10 OR HYDROXYNEFAZODONE/OBI
L19           2 SEA FILE=CAPLUS ABB=ON  L14 OR OXONEFAZODONE/OBI
L20        2952 SEA FILE=CAPLUS ABB=ON  L16 OR FLUOXETINE/OBI
L28       28703 SEA FILE=CAPLUS ABB=ON  DRUG INTERACTIONS+OLD,NT/CT
L29      134211 SEA FILE=CAPLUS ABB=ON  DRUG DELIVERY SYSTEMS+OLD/CT
L30        2123 SEA FILE=CAPLUS ABB=ON  L29(L)COMB?
L33          19 SEA FILE=CAPLUS ABB=ON  (L17 OR L18 OR L19)(L)COMB?
L34         110 SEA FILE=CAPLUS ABB=ON  L20(L)COMB?
L143          5 SEA FILE=CAPLUS ABB=ON  L33 AND L34 AND (L28 OR L30)

=> fil medl; d que nos 158; d que nos 165

FILE 'MEDLINE' ENTERED AT 16:41:30 ON 03 OCT 2003

 FILE LAST UPDATED: 2 OCT 2003 (20031002/UP).  FILE COVERS 1958 TO DATE.

 On April 13, 2003, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary.  See http://www.nlm.nih.gov/mesh/changes2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

L58           0 SEA FILE=MEDLINE ABB=ON  OXONEFAZODONE
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L55        4299 SEA FILE=MEDLINE ABB=ON  FLUOXETINE/CT
L56         355 SEA FILE=MEDLINE ABB=ON  NEFAZODONE/CN
L57          14 SEA FILE=MEDLINE ABB=ON  HYDROXYNEFAZODONE/CN
L62       72636 SEA FILE=MEDLINE ABB=ON  DRUG THERAPY, COMBINATION/CT
L63       94170 SEA FILE=MEDLINE ABB=ON  DRUG INTERACTIONS+NT/CT
L64       35998 SEA FILE=MEDLINE ABB=ON  DRUG COMBINATIONS/CT
L65           6 SEA FILE=MEDLINE ABB=ON  L55 AND (L56 OR L57) AND (L62 OR L63
                OR L64)

=> fil embase; d que nos l73; d que nos l80; d que nos l94

FILE 'EMBASE' ENTERED AT 16:41:31 ON 03 OCT 2003
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 FILE COVERS 1974 TO 2 Oct 2003 (20031002/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

L73           0 SEA FILE=EMBASE ABB=ON  OXONEFAZODONE


L70       14776 SEA FILE=EMBASE ABB=ON  FLUOXETINE/CT
L71        2077 SEA FILE=EMBASE ABB=ON  NEFAZODONE/CT
L72          33 SEA FILE=EMBASE ABB=ON  HYDROXYNEFAZODONE/CT
L76        1139 SEA FILE=EMBASE ABB=ON  L70(L)CB/CT
L77         157 SEA FILE=EMBASE ABB=ON  ((L71 OR L72))(L)CB/CT
L78          54 SEA FILE=EMBASE ABB=ON  L76 AND L77
L79        4072 SEA FILE=EMBASE ABB=ON  COMBINATION CHEMOTHERAPY/CT
L80           4 SEA FILE=EMBASE ABB=ON  L78 AND L79


L70       14776 SEA FILE=EMBASE ABB=ON  FLUOXETINE/CT
L71        2077 SEA FILE=EMBASE ABB=ON  NEFAZODONE/CT
L72          33 SEA FILE=EMBASE ABB=ON  HYDROXYNEFAZODONE/CT
L76        1139 SEA FILE=EMBASE ABB=ON  L70(L)CB/CT
L77         157 SEA FILE=EMBASE ABB=ON  ((L71 OR L72))(L)CB/CT
L78          54 SEA FILE=EMBASE ABB=ON  L76 AND L77
L90      162652 SEA FILE=EMBASE ABB=ON  DRUG INTERACTION+NT/CT
L92          27 SEA FILE=EMBASE ABB=ON  L78 AND L90
L94          10 SEA FILE=EMBASE ABB=ON  L92 AND (DANGEROUS OR SYNERGISM OR
                INTERACTIONS OR REFRACTORY)/TI


=> s l80 or l94

L147         14 L80 OR L94

=> fil drugu; d que nos l125; d que nos l139

FILE 'DRUGU' ENTERED AT 16:41:32 ON 03 OCT 2003
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FILE LAST UPDATED: 2 OCT 2003       <20031002/UP>
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>>>  DERWENT DRUG FILE (SUBSCRIBER)  <<<

>>>  SDI'S MAY BE RUN WEEKLY OR MONTHLY AS OF JUNE 2001.  <<<
>>>  (WEEKLY IS THE DEFAULT). FOR PRICING INFORMATION     <<<
>>>  SEE HELP COST                                        <<<

>>>  FILE COVERS 1983 TO DATE  <<<
>>>  THESAURUS AVAILABLE IN /CT  <<<


L125           0 SEA FILE=DRUGU ABB=ON  OXONEFAZODONE



L122        5746 SEA FILE=DRUGU ABB=ON  FLUOXETINE/CT
L123         703 SEA FILE=DRUGU ABB=ON  NEFAZODONE/CT
L124          52 SEA FILE=DRUGU ABB=ON  HYDROXYNEFAZODONE/CT
L127         356 SEA FILE=DRUGU ABB=ON  L122 AND (L123 OR L124)
L128      111523 SEA FILE=DRUGU ABB=ON  COMB./CT
L138       37864 SEA FILE=DRUGU ABB=ON  DRUG INTERACTIONS/CC
L139           8 SEA FILE=DRUGU ABB=ON  L127 AND L128 AND L138


=> dup rem l65,l139,l143,l147
FILE 'MEDLINE' ENTERED AT 16:41:49 ON 03 OCT 2003

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PROCESSING COMPLETED FOR L65
PROCESSING COMPLETED FOR L139
PROCESSING COMPLETED FOR L143
PROCESSING COMPLETED FOR L147
L148          30 DUP REM L65 L139 L143 L147 (3 DUPLICATES REMOVED)
                 ANSWERS '1-6' FROM FILE MEDLINE
                 ANSWERS '7-13' FROM FILE DRUGU
                 ANSWERS '14-18' FROM FILE CAPLUS
                 ANSWERS '19-30' FROM FILE EMBASE

=> d iall 1-13; d ibib ab hitrn 14-18; d iall 19-30; fil hom

L148 ANSWER 1 OF 30     MEDLINE on STN                DUPLICATE 2
ACCESSION NUMBER:    2000352681     MEDLINE
DOCUMENT NUMBER:     20352681   PubMed ID: 10896409
TITLE:               Terfenadine-antidepressant interactions: an in vitro
                     inhibition study using human liver microsomes.
AUTHOR:              Jurima-Romet M; Wright M; Neigh S
CORPORATE SOURCE:    Bureau of Drug Research, Therapeutic Products Directorate,
                     Health Canada, Ottawa, Canada.
SOURCE:              BRITISH JOURNAL OF CLINICAL PHARMACOLOGY, (1998 Mar) 45 (3)
                     318-21.
                     Journal code: 7503323. ISSN: 0306-5251.
PUB. COUNTRY:        ENGLAND: United Kingdom
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
```

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000720
Last Updated on STN: 20000720
Entered Medline: 20000711

ABSTRACT:
AIMS: Inhibition of the metabolism of terfenadine has been associated with torsades de pointes ventricular arrhythmias. The aim of this study was to assess in vitro the potency of the antidepressants nefazodone, sertraline and fluoxetine in inhibiting terfenadine biotransformation. METHODS: Human liver microsomes were incubated with terfenadine and the antidepressants at various concentrations. Formation of the two major metabolites of terfenadine was determined by h.p.l.c. RESULTS: The apparent Km for microsomes from four human livers was 11+/-5 and 18+/-3 microM (mean +/-s.e.mean) for the N-dealkylation and C-hydroxylation pathways, respectively. Nefazodone, sertraline and fluoxetine inhibited terfenadine N-dealkylation with K(i) values of 10+/-4, 10+/-3 and 68+/-15 microM respectively. Inhibition of the C-hydroxylation pathway yielded noncompetitive K(i) values of 41+/-4, 67+/-13 and 310+/-40 microM respectively. CONCLUSIONS: Nefazodone and sertraline were moderately weak in vitro inhibitors of terfenadine metabolism while fluoxetine was a very weak inhibitor. Clinically significant interaction of terfenadine is more likely with nefazodone than sertraline or fluoxetine since therapeutic plasma levels of nefazodone are comparatively higher.

CONTROLLED TERM: Check Tags: Comparative Study; Human
Alkylation
*Antidepressive Agents, Second-Generation: PD, pharmacology
Biotransformation: DE, drug effects
Chromatography, High Pressure Liquid
Cytochrome P-450 Enzyme System: ME, metabolism
Drug Interactions
Fluoxetine: PD, pharmacology
*Histamine H1 Antagonists: PK, pharmacokinetics
Hydroxylation
Microsomes, Liver: DE, drug effects
*Microsomes, Liver: ME, metabolism
Mixed Function Oxygenases: ME, metabolism
Sertraline: PD, pharmacology
*Terfenadine: PK, pharmacokinetics
Triazoles: PD, pharmacology

CAS REGISTRY NO.: 50679-08-8 (Terfenadine); 54910-89-3 (Fluoxetine); 79617-96-2 (Sertraline); **83366-66-9 (nefazodone)**; 9035-51-2 (Cytochrome P-450 Enzyme System)

CHEMICAL NAME: 0 (Antidepressive Agents, Second-Generation); 0 (Histamine H1 Antagonists); 0 (Triazoles); EC 1.- (Mixed Function Oxygenases); EC 1.14.14.1 (nifedipine oxidase)

L148 ANSWER 2 OF 30 MEDLINE on STN
ACCESSION NUMBER: 2000194804 MEDLINE
DOCUMENT NUMBER: 20194804 PubMed ID: 10732666
TITLE: A case report of serotonin syndrome associated with combined nefazodone and fluoxetine.
AUTHOR: Smith D L; Wenegrat B G
SOURCE: JOURNAL OF CLINICAL PSYCHIATRY, (2000 Feb) 61 (2) 146.
Journal code: 7801243. ISSN: 0160-6689.
PUB. COUNTRY: United States
DOCUMENT TYPE: Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000407
Last Updated on STN: 20000407
Entered Medline: 20000328
CONTROLLED TERM: Check Tags: Case Report; Human; Male

*Antidepressive Agents, Second-Generation: AE, adverse effects
Antidepressive Agents, Second-Generation: TU, therapeutic use
Bipolar Disorder: DT, drug therapy
Drug Therapy, Combination
***Fluoxetine: AE, adverse effects**
Fluoxetine: TU, therapeutic use
Middle Age
*Serotonin Syndrome: CI, chemically induced
Serotonin Syndrome: ME, metabolism
*Serotonin Uptake Inhibitors: AE, adverse effects
Serotonin Uptake Inhibitors: TU, therapeutic use
*Triazoles: AE, adverse effects
Triazoles: TU, therapeutic use
CAS REGISTRY NO.: 54910-89-3 (Fluoxetine); **83366-66-9 (nefazodone)**
CHEMICAL NAME: 0 (Antidepressive Agents, Second-Generation); 0 (Serotonin Uptake Inhibitors); 0 (Triazoles)

L148 ANSWER 3 OF 30 MEDLINE on STN
ACCESSION NUMBER: 2001012596 MEDLINE
DOCUMENT NUMBER: 20453059 PubMed ID: 10997936
TITLE: CYP2B6 mediates the in vitro hydroxylation of bupropion: potential drug interactions with other antidepressants.
AUTHOR: Hesse L M; Venkatakrishnan K; Court M H; von Moltke L L; Duan S X; Shader R I; Greenblatt D J
CORPORATE SOURCE: Department of Pharmacology and Experimental Therapeutics, Tufts University School of Medicine, and the Division of Clinical Pharmacology, New England Medical Center, Boston, Massachusetts, USA.
CONTRACT NUMBER: MH01237 (NIMH)
MH34223 (NIMH)
RR00054 (NCRR)
+
SOURCE: DRUG METABOLISM AND DISPOSITION, (2000 Oct) 28 (10) 1176-83.
Journal code: 9421550. ISSN: 0090-9556.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001101

ABSTRACT:
The in vitro biotransformation of bupropion to hydroxybupropion was studied in human liver microsomes and microsomes containing heterologously expressed human cytochromes P450 (CYP). The mean (+/-S.E.) K(m) in four human liver microsomes was 89 (+/-14) microM. In microsomes containing cDNA-expressed CYPs, hydroxybupropion formation was mediated only by CYP2B6 at 50 microM bupropion (K(m) 85 microM). A CYP2B6 inhibitory antibody produced more than 95% inhibition of bupropion hydroxylation in four human livers. Bupropion hydroxylation activity at 250 microM was highly correlated with S-mephenytoin N-demethylation activity (yielding nirvanol), another CYP2B6-mediated reaction, in a panel of 32 human livers (r = 0.94). The CYP2B6 content of 12 human livers highly correlated with bupropion hydroxylation activity (r = 0.96). Thus bupropion hydroxylation is mediated almost exclusively by CYP2B6 and can serve as an index reaction reflecting activity of this isoform. IC(50) values for inhibition of a CYP2D6 index reaction (dextromethorphan O-demethylation) by bupropion and hydroxybupropion were 58 and 74 microM, respectively. This suggests a low inhibitory potency versus CYP2D6, the clinical importance of which is not established. Since bupropion is frequently coadministered with

other antidepressants, IC(50) values (microM) for inhibition of bupropion hydroxylation were determined as follows: paroxetine (1.6), fluvoxamine (6.1), sertraline (3.2), desmethylsertraline (19.9), fluoxetine (59.5), norfluoxetine (4.2), and nefazodone (25.4). Bupropion hydroxylation was only weakly inhibited by venlafaxine, O-desmethylvenlafaxine, citalopram, and desmethylcitalopram. The inhibition of bupropion hydroxylation in vitro by a number of newer antidepressants suggests the potential for clinical drug interactions.

CONTROLLED TERM: Check Tags: Human; Support, U.S. Gov't, P.H.S.
Antibodies: PD, pharmacology
*Antidepressive Agents, Second-Generation: ME, metabolism
Antidepressive Agents, Second-Generation: PK, pharmacokinetics
Biotransformation
*Bupropion: ME, metabolism
Bupropion: PK, pharmacokinetics
Chromatography, High Pressure Liquid
Cytochrome P-450 Enzyme System: IM, immunology
*Cytochrome P-450 Enzyme System: ME, metabolism
Dose-Response Relationship, Drug
Drug Interactions
***Fluoxetine: AA, analogs & derivatives**
Fluoxetine: PD, pharmacology
Fluvoxamine: PD, pharmacology
Hydroxylation: DE, drug effects
Isoenzymes: ME, metabolism
Kinetics
Microsomes, Liver: ME, metabolism
Oxidoreductases, N-Demethylating: IM, immunology
*Oxidoreductases, N-Demethylating: ME, metabolism
Paroxetine: PD, pharmacology
*Sertraline: AA, analogs & derivatives
Sertraline: PD, pharmacology
Triazoles: PD, pharmacology

CAS REGISTRY NO.: 34841-39-9 (Bupropion); 54739-18-3 (Fluvoxamine); 54910-89-3 (Fluoxetine); 56161-73-0 (norfluoxetine); 61869-08-7 (Paroxetine); 79617-96-2 (Sertraline); **83366-66-9 (nefazodone)**; 87857-41-8 (CP 53261); 9035-51-2 (Cytochrome P-450 Enzyme System)

CHEMICAL NAME: 0 (Antibodies); 0 (Antidepressive Agents, Second-Generation); 0 (Isoenzymes); 0 (Triazoles); EC 1.14.14.1 (S-mephenytoin N-demethylase); EC 1.5. (Oxidoreductases, N-Demethylating)

L148 ANSWER 4 OF 30 MEDLINE on STN
ACCESSION NUMBER: 1998385433 MEDLINE
DOCUMENT NUMBER: 98385433 PubMed ID: 9720479
TITLE: Pharmacokinetic interactions of antidepressants.
AUTHOR: Richelson E
CORPORATE SOURCE: Department of Psychiatry and Pharmacology, Mayo Medical School, Rochester, Minn, USA.
SOURCE: JOURNAL OF CLINICAL PSYCHIATRY, (1998) 59 Suppl 10 22-6. Ref: 32
Journal code: 7801243. ISSN: 0160-6689.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980910
Last Updated on STN: 19980910

Entered Medline: 19980828

ABSTRACT:
Seven of the newest antidepressants are the serotonin selective reuptake inhibitors (fluoxetine, sertraline, paroxetine, and fluvoxamine [currently approved in the United States for obsessive-compulsive disorder only]), a serotonin norepinephrine reuptake inhibitor (venlafaxine), a postsynaptic serotonin antagonist/presynaptic serotonin reuptake inhibitor (nefazodone), and presynaptic/postsynaptic noradrenergic/serotonergic receptor antagonist (mirtazapine). Many of these drugs are potent inhibitors of the cytochrome P450 (CYP) enzymes of the liver. The CYP enzymes most relevant to the use of antidepressants and for which the most thorough data are available are the CYP1A2, CYP2D6, and CYP3A4. These 3 CYP isoenzymes are discussed in relation to some of the drugs they metabolize, and appropriate cautions are recommended for concurrent administration of these new antidepressants and other drugs frequently prescribed to elderly patients.

CONTROLLED TERM: Check Tags: Human
Antidepressive Agents: AE, adverse effects
*Antidepressive Agents: PK, pharmacokinetics
Cyclohexanols: AE, adverse effects
Cyclohexanols: PK, pharmacokinetics
Cytochrome P-450 CYP1A2: DE, drug effects
Cytochrome P-450 CYP2D6: DE, drug effects
Cytochrome P-450 Enzyme System: DE, drug effects
*Depressive Disorder: DT, drug therapy
Drug Interactions
Drug Therapy, Combination
Fluoxetine: AE, adverse effects
Fluoxetine: PK, pharmacokinetics
Fluvoxamine: AE, adverse effects
Fluvoxamine: PK, pharmacokinetics
Mixed Function Oxygenases: DE, drug effects
Serotonin Uptake Inhibitors: AE, adverse effects
Serotonin Uptake Inhibitors: PK, pharmacokinetics
Triazoles: AE, adverse effects
Triazoles: PK, pharmacokinetics

CAS REGISTRY NO.: 54739-18-3 (Fluvoxamine); 54910-89-3 (Fluoxetine); **83366-66-9 (nefazodone)**; 9035-51-2 (Cytochrome P-450 Enzyme System); 93413-69-5 (venlafaxine)

CHEMICAL NAME: 0 (Antidepressive Agents); 0 (Cyclohexanols); 0 (Serotonin Uptake Inhibitors); 0 (Triazoles); EC 1.- (Mixed Function Oxygenases); EC 1.14.14.1 (Cytochrome P-450 CYP1A2); EC 1.14.14.1 (Cytochrome P-450 CYP2D6); EC 1.14.14.1 (nifedipine oxidase)

L148 ANSWER 5 OF 30 MEDLINE on STN
ACCESSION NUMBER: 97352101 MEDLINE
DOCUMENT NUMBER: 97352101 PubMed ID: 9208383
TITLE: Dangerous interaction with nefazodone added to fluoxetine, desipramine, venlafaxine, valproate and clonazepam combination therapy.
AUTHOR: Benazzi F
SOURCE: JOURNAL OF PSYCHOPHARMACOLOGY, (1997) 11 (2) 190-1. Journal code: 8907828. ISSN: 0269-8811.
PUB. COUNTRY: United States
DOCUMENT TYPE: Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199708
ENTRY DATE: Entered STN: 19970825
Last Updated on STN: 19990129
Entered Medline: 19970812
CONTROLLED TERM: Check Tags: Case Report; Female; Human
Adult

Antidepressive Agents: AD, administration & dosage
*Antidepressive Agents: AE, adverse effects
Clonazepam: AD, administration & dosage
*Clonazepam: AE, adverse effects
Cyclohexanols: AD, administration & dosage
*Cyclohexanols: AE, adverse effects
*Depressive Disorder: DT, drug therapy
Depressive Disorder: PX, psychology
Desipramine: AD, administration & dosage
*Desipramine: AE, adverse effects
Drug Therapy, Combination
Fluoxetine: AD, administration & dosage
***Fluoxetine: AE, adverse effects**
*Hypotension: CI, chemically induced
*Panic Disorder: DT, drug therapy
Panic Disorder: PX, psychology
Substance Withdrawal Syndrome: ET, etiology
Triazoles: AD, administration & dosage
*Triazoles: AE, adverse effects

CAS REGISTRY NO.: 1622-61-3 (Clonazepam); 50-47-5 (Desipramine); 54910-89-3 (Fluoxetine); **83366-66-9 (nefazodone)**; 93413-69-5 (venlafaxine)
CHEMICAL NAME: 0 (Antidepressive Agents); 0 (Cyclohexanols); 0 (Triazoles)

L148 ANSWER 6 OF 30 MEDLINE on STN
ACCESSION NUMBER: 96218852 MEDLINE
DOCUMENT NUMBER: 96218852 PubMed ID: 8626361
TITLE: The safety profile of nefazodone.
COMMENT: Comment in: J Clin Psychiatry. 2000 Mar;61(3):216-7
AUTHOR: Robinson D S; Roberts D L; Smith J M; Stringfellow J C; Kaplita S B; Seminara J A; Marcus R N
CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, CT 06492, USA.
SOURCE: JOURNAL OF CLINICAL PSYCHIATRY, (1996) 57 Suppl 2 31-8.
Ref: 20
Journal code: 7801243. ISSN: 0160-6689.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960708
Last Updated on STN: 20000810
Entered Medline: 19960625

ABSTRACT:
Comprehensive review of safety data from approximately 3500 patients who received nefazodone in premarketing clinical trials demonstrates the drug to be very well tolerated, with a favorable side effect profile compared with other antidepressant drugs. Nefazodone treatment was associated with fewer side effects than were the control drugs. The incidence of side effects was generally low, and treatment discontinuations for adverse effects were less frequent with nefazodone than with imipramine and comparable with fluoxetine. No late-appearing side effects or toxicity emerged during the long-term treatment (1 year or longer) of several hundred patients. There were no drug-related fatalities and no evidence that nefazodone caused specific organ toxicity, although some cardiovascular side effects were noted (e.g., asymptomatic reduced systolic blood pressure, asymptomatic sinus bradycardia). Experience in 488 elderly patients treated with nefazodone yielded no evidence of increased susceptibility of older patients to nefazodone-associated adverse experiences, including those pertaining to the cardiovascular system. However, treatment should be initiated at a reduced dose in elderly patients because of

reduced hepatic clearance of nefazodone in this age group. Final dose range may be similar in healthy younger and older patients. Although nefazodone may interact with some other medications (e.g., increases at steady state in AUC: alprazolam, twofold; triazolam, fourfold), drug-drug interactions involving patients have been clinically minor. On the basis of the inhibition of cytochrome P450 3A4 isoenzyme by nefazodone in vitro, coadministration of terfenadine or astemizole with nefazodone is contraindicated because nefazodone can increase the plasma levels of these two drugs. Extensive clinical experience provides substantial evidence that nefazodone is an extremely safe and effective treatment for depression, with important advantages over existing therapies. Therapeutic benefits include a low incidence of clinically troublesome side effects and lack of unwanted psychic activation, sexual dysfunction, weight change, and the cardiotoxicity of other antidepressants.

CONTROLLED TERM: Check Tags: Female; Human; Male
Adolescent
Adult
Age Factors
Aged
*Antidepressive Agents, Second-Generation: AE, adverse effects
Antidepressive Agents, Second-Generation: TU, therapeutic use
Antidepressive Agents, Tricyclic: AE, adverse effects
Clinical Trials
Cytochrome P-450 Enzyme System: DE, drug effects
Depressive Disorder: DT, drug therapy
Depressive Disorder: PX, psychology
Double-Blind Method
Drug Interactions
Fluoxetine: AE, adverse effects
Imipramine: AE, adverse effects
Middle Age
Mixed Function Oxygenases: DE, drug effects
Placebos
Sexual Dysfunctions, Psychological: CI, chemically induced
Treatment Outcome
*Triazoles: AE, adverse effects
Triazoles: TU, therapeutic use
Weight Gain

CAS REGISTRY NO.: 50-49-7 (Imipramine); 54910-89-3 (Fluoxetine); **83366-66-9 (nefazodone)**; 9035-51-2 (Cytochrome P-450 Enzyme System)

CHEMICAL NAME: 0 (Antidepressive Agents, Second-Generation); 0 (Antidepressive Agents, Tricyclic); 0 (Placebos); 0 (Triazoles); EC 1.- (Mixed Function Oxygenases); EC 1.14.14.1 (nifedipine oxidase)

L148 ANSWER 7 OF 30 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 1
ACCESSION NUMBER: 1999-00760 DRUGU T S
TITLE: Serotonin syndrome resulting from drug interactions.
AUTHOR: Chan B S H; G; A; Whyte I M; Dawson A H; Braitberg G; Duggin G G
LOCATION: Randwick, Westmead, Newcastle and Heidelberg, Austr.
SOURCE: Med.J.Aust. (169, No. 10, 523-25, 1998) 15 Ref.
CODEN: MJAUAJ ISSN: 0025-729X
AVAIL. OF DOC.: Reprints Not Available. Department of Emergency Medicine, Prince of Wales Hospital, Barker Street, Randwick, NSW 2031, Australia.
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

6 Cases of serotonin syndrome following drug interactions (clomipramine and moclobemide, desipramine and paroxetine, venlafaxine and paroxetine, amitriptyline with thioridazine and nefazodone, moclobemide with diazepam and venlafaxine, fluoxetine and moclobemide) were reported. All 6 patients presented with serotonin syndrome after taking different drugs while on treatment with other agents, or after switching drugs without a proper washout period. All patients recovered, most after treatment with cyproheptadine or nitrazepam. Further investigation is necessary to examine the treatment of serotonin syndrome, but care must be taken with patients for interaction of serotonergic drugs and signs and symptoms, must be examined.

SECTION HEADING: T Therapeutics
S Adverse Effects

CLASSIF. CODE: 35 Adverse Reactions
60 Autonomic
66 Drug Interactions

CONTROLLED TERM:
CASE-HISTORY *FT; IN-VIVO *FT; CASES *FT
[01] CLOMIPRAMINE *AE; CLOMIPRAMINE *DI; SEROTONIN-SYNDROME *AE; AGITATION *AE; CONFUSION *AE; MANIA *AE; DIAPHORESIS *AE; PYREXIA *AE; HYPERREFLEXIA *AE; DIZZINESS *AE; MYOCLONUS *AE; TREMOR *AE; MENTAL-DISORDER *AE; MENTAL-DISORDER *AE; PSYCHOSIS *AE; SWEAT *AE; SPINAL-CORD-DISEASE *AE; EPILEPSY *AE; ENCEPHALOPATHY *AE; MOCLOBEMIDE *DI; CLOMIPRAM *RN; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; AE *FT; DI *FT
CAS REGISTRY NO.: 303-49-1
[02] DESIPRAMINE *AE; DESIPRAMINE *DI; SEROTONIN-SYNDROME *AE; AGITATION *AE; CONFUSION *AE; MANIA *AE; DIAPHORESIS *AE; PYREXIA *AE; HYPERREFLEXIA *AE; DIZZINESS *AE; MYOCLONUS *AE; TREMOR *AE; MENTAL-DISORDER *AE; MENTAL-DISORDER *AE; PSYCHOSIS *AE; SWEAT *AE; SPINAL-CORD-DISEASE *AE; EPILEPSY *AE; ENCEPHALOPATHY *AE; PAROXETINE *DI; DESIPRAMI *RN; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; AE *FT; DI *FT
CAS REGISTRY NO.: 50-47-5
[03] PAROXETINE *AE; PAROXETINE *DI; SEROTONIN-SYNDROME *AE; AGITATION *AE; CONFUSION *AE; MANIA *AE; DIAPHORESIS *AE; PYREXIA *AE; HYPERREFLEXIA *AE; DIZZINESS *AE; MYOCLONUS *AE; TREMOR *AE; MENTAL-DISORDER *AE; MENTAL-DISORDER *AE; PSYCHOSIS *AE; SWEAT *AE; SPINAL-CORD-DISEASE *AE; EPILEPSY *AE; ENCEPHALOPATHY *AE; VENLAFAXINE *DI; DESIPRAMINE *DI; PAROXETIN *RN; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; AE *FT; DI *FT
CAS REGISTRY NO.: 61869-08-7
[04] AMITRIPTYLINE *AE; AMITRIPTYLINE *DI; SEROTONIN-SYNDROME *AE; AGITATION *AE; CONFUSION *AE; MANIA *AE; DIAPHORESIS *AE; PYREXIA *AE; HYPERREFLEXIA *AE; DIZZINESS *AE; MYOCLONUS *AE; TREMOR *AE; MENTAL-DISORDER *AE; MENTAL-DISORDER *AE; PSYCHOSIS *AE; SWEAT *AE; SPINAL-CORD-DISEASE *AE; EPILEPSY *AE; ENCEPHALOPATHY *AE; **NEFAZODONE** *DI; AMITRIPTY *RN; **COMB**. *FT; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; AE *FT; DI *FT
CAS REGISTRY NO.: 50-48-6
[05] THIORIDAZINE *AE; THIORIDAZINE *DI; SEROTONIN-SYNDROME *AE; AGITATION *AE; CONFUSION *AE; MANIA *AE; DIAPHORESIS *AE; PYREXIA *AE; HYPERREFLEXIA *AE; DIZZINESS *AE; MYOCLONUS *AE; TREMOR *AE; MENTAL-DISORDER *AE; MENTAL-DISORDER *AE; PSYCHOSIS *AE; SWEAT *AE; SPINAL-CORD-DISEASE *AE; EPILEPSY *AE; ENCEPHALOPATHY *AE; **NEFAZODONE** *DI; THIORIDAZ *RN; **COMB**. *FT; PSYCHOSEDATIVES *FT; NEUROLEPTICS *FT; DOPAMINE-ANTAGONISTS *FT; CALMODULIN-ANTAGONISTS *FT; AE *FT; DI *FT

CAS REGISTRY NO.: 50-52-2
[06] **NEFAZODONE** *AE; **NEFAZODONE** *DI; SEROTONIN-SYNDROME *AE; AGITATION *AE; CONFUSION *AE; MANIA *AE; DIAPHORESIS *AE; PYREXIA *AE; HYPERREFLEXIA *AE; DIZZINESS *AE; MYOCLONUS *AE; TREMOR *AE; MENTAL-DISORDER *AE; MENTAL-DISORDER *AE; PSYCHOSIS *AE; SWEAT *AE; SPINAL-CORD-DISEASE *AE; EPILEPSY *AE; ENCEPHALOPATHY *AE; AMITRIPTYLINE *DI; THIORIDAZINE *DI; NEFAZODON *RN; ANTIDEPRESSANTS *FT; PSYCHOSTIMULANTS *FT; AE *FT; DI *FT

CAS REGISTRY NO.: 83366-66-9
[07] VENLAFAXINE *AE; VENLAFAXINE *DI; SEROTONIN-SYNDROME *AE; AGITATION *AE; CONFUSION *AE; MANIA *AE; DIAPHORESIS *AE; PYREXIA *AE; HYPERREFLEXIA *AE; DIZZINESS *AE; MYOCLONUS *AE; TREMOR *AE; MENTAL-DISORDER *AE; MENTAL-DISORDER *AE; PSYCHOSIS *AE; SWEAT *AE; SPINAL-CORD-DISEASE *AE; EPILEPSY *AE; ENCEPHALOPATHY *AE; DIAZEPAM *DI; MOCLOBEMIDE *DI; PAROXETINE *DI; WY-45030 *RN; ANTIDEPRESSANTS *FT; PSYCHOSTIMULANTS *FT; AE *FT; DI *FT

CAS REGISTRY NO.: 99300-78-4
[08] DIAZEPAM *AE; DIAZEPAM *DI; SEROTONIN-SYNDROME *AE; AGITATION *AE; CONFUSION *AE; MANIA *AE; DIAPHORESIS *AE; PYREXIA *AE; HYPERREFLEXIA *AE; DIZZINESS *AE; MYOCLONUS *AE; TREMOR *AE; MENTAL-DISORDER *AE; MENTAL-DISORDER *AE; PSYCHOSIS *AE; SWEAT *AE; SPINAL-CORD-DISEASE *AE; EPILEPSY *AE; ENCEPHALOPATHY *AE; VENLAFAXINE *DI; DIAZEPAM *RN; **COMB.** *FT; SEDATIVES *FT; RELAXANTS *FT; PSYCHOSEDATIVES *FT; TRANQUILIZERS *FT; BENZODIAZEPINE-AGONISTS *FT; AE *FT; DI *FT

CAS REGISTRY NO.: 439-14-5
[09] **FLUOXETINE** *AE; **FLUOXETINE** *DI; SEROTONIN-SYNDROME *AE; AGITATION *AE; CONFUSION *AE; MANIA *AE; DIAPHORESIS *AE; PYREXIA *AE; HYPERREFLEXIA *AE; DIZZINESS *AE; MYOCLONUS *AE; TREMOR *AE; MENTAL-DISORDER *AE; MENTAL-DISORDER *AE; PSYCHOSIS *AE; SWEAT *AE; SPINAL-CORD-DISEASE *AE; EPILEPSY *AE; ENCEPHALOPATHY *AE; MOCLOBEMIDE *DI; FLUOXETIN *RN; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; AE *FT; DI *FT

CAS REGISTRY NO.: 54910-89-3
[10] MOCLOBEMIDE *DI; MOCLOBEMIDE *AE; SEROTONIN-SYNDROME *AE; AGITATION *AE; CONFUSION *AE; MANIA *AE; DIAPHORESIS *AE; PYREXIA *AE; HYPERREFLEXIA *AE; DIZZINESS *AE; MYOCLONUS *AE; TREMOR *AE; MENTAL-DISORDER *AE; MENTAL-DISORDER *AE; PSYCHOSIS *AE; SWEAT *AE; SPINAL-CORD-DISEASE *AE; EPILEPSY *AE; ENCEPHALOPATHY *AE; **FLUOXETINE** *DI; VENLAFAXINE *DI; CLOMIPRAMINE *DI; MOCLOBEMI *RN; **COMB.** *FT; ANTIDEPRESSANTS *FT; PSYCHOSTIMULANTS *FT; MAO-INHIBITORS *FT; DI *FT; AE *FT

CAS REGISTRY NO.: 71320-77-9
[11] CYPROHEPTADINE *TR; SEROTONIN-SYNDROME *TR; AGITATION *TR; CONFUSION *TR; MANIA *TR; DIAPHORESIS *TR; PYREXIA *TR; HYPERREFLEXIA *TR; DIZZINESS *TR; MYOCLONUS *TR; TREMOR *TR; MENTAL-DISORDER *TR; MENTAL-DISORDER *TR; PSYCHOSIS *TR; SWEAT *TR; SPINAL-CORD-DISEASE *TR; EPILEPSY *TR; ENCEPHALOPATHY *TR; CYPROHEPT *RN; ANTISEROTONIN *FT; ANTIHISTAMINES-H1 *FT; TONICS *FT; ANTISEROTONINS *FT; TR *FT

CAS REGISTRY NO.: 129-03-3
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L148 ANSWER 8 OF 30 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-23139 DRUGU T P S
TITLE: Strategies for optimizing antiepileptic drug therapy in elderly people.

AUTHOR: Lackner T E
CORPORATE SOURCE: Univ.Minnesota
LOCATION: Minneapolis, Minn., USA
SOURCE: Pharmacotherapy (22, No. 3, 329-64, 2002) 7 Tab. 301 Ref.
CODEN: PHPYDQ ISSN: 0277-0008
AVAIL. OF DOC.: College of Pharmacy, University of Minnesota, Weaver-Densford Hall, Suite 7-115E, 308 Harvard Street SE, Minneapolis, MN 55455, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

Strategies for optimizing antiepileptic drug (AED) therapy in the elderly are reviewed with reference to the traditional AED: phenytoin, fosphenytoin, carbamazepine, diazepam, clonazepam, valproate, phenobarbital and primidone, and the newer AED: felbamate, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, tiagabine, topiramate and zonisamide. Use of AED in agitation and aggression of dementia, bipolar disorder, essential tremor and neuropathic pain, as well as in epilepsy, is considered. Adverse drug reactions (ADR), drug interactions, serum AED concentration monitoring and economic considerations are also discussed.

SECTION HEADING: T Therapeutics
P Pharmacology
S Adverse Effects

CLASSIF. CODE: 8 Pharmacokinetics
35 Adverse Reactions
59 CNS and Motor
66 Drug Interactions
67 Children and Elderly
69 Reviews

CONTROLLED TERM:

EPILEPSY *TR; ENCEPHALOPATHY *TR; CASES *FT; GERIATRICS *FT; IN-VIVO *FT; ANTICONVULSANT *FT; SAFETY *FT; REVIEW *FT
[01] MAIN-TOPIC *FT; ANTICONVULSANTS *FT; TR *FT; AE *FT
[02] BIPOLAR *TR; DEPRESSION *TR; DEMENTIA *TR; NEUROPATHIC *TR; PAIN *TR; TREMOR *TR; MENTAL-DISORDER *TR; PSYCHOSIS *TR; PHENYTOIN *TR; FOSPHENYTOIN *TR; CARBAMAZEPINE *TR; DIAZEPAM *TR; CLONAZEPAM *TR; VALPROATE *TR; PHENOBARBITAL *TR; PRIMIDONE *TR; FELBAMATE *TR; GABAPENTIN *TR; LAMOTRIGINE *TR; LEVETIRACETAM *TR; OXCARBAZEPINE *TR; TIAGABINE *TR; TOPIRAMATE *TR; ZONISAMIDE *TR; PHENYTOIN *AE; FOSPHENYTOIN *AE; CARBAMAZEPINE *AE; DIAZEPAM *AE; CLONAZEPAM *AE; VALPROATE *AE; PHENOBARBITAL *AE; PRIMIDONE *AE; FELBAMATE *AE; GABAPENTIN *AE; LAMOTRIGINE *AE; LEVETIRACETAM *AE; OXCARBAZEPINE *AE; TIAGABINE *AE; TOPIRAMATE *AE; ZONISAMIDE *AE; PHENYTOIN *DM; FOSPHENYTOIN *DM; CARBAMAZEPINE *DM; DIAZEPAM *DM; CLONAZEPAM *DM; VALPROATE *DM; PHENOBARBITAL *DM; PRIMIDONE *DM; FELBAMATE *DM; GABAPENTIN *DM; LAMOTRIGINE *DM; LEVETIRACETAM *DM; OXCARBAZEPINE *DM; TIAGABINE *DM; TOPIRAMATE *DM; ZONISAMIDE *DM; ANTIMANIC *FT; COST *FT; ANALGESIC *FT; DOSAGE *FT; PHARMACOKINETICS *FT; PHARMACODYNAMICS *FT; ECONOMICS *FT; TR *FT; AE *FT; DI *FT; DM *FT
[03] ATAXIA *AE; DIZZINESS *AE; DROWSINESS *AE; DIPLOPIA *AE; HYPONATREMIA *AE; NAUSEA *AE; EMESIS *AE; HEADACHE *AE; ANOREXIA *AE; DYSPEPSIA *AE; ASTHENIA *AE; DROWSINESS *AE; CONSTIPATION *AE; HYPOTÉNSION *AE; NYSTAGMUS *AE; TREMOR *AE; EDEMA *AE; WEIGHT-GAIN *AE; INSOMNIA *AE; INCOORDINATION *AE; DEPRESSION *AE; ANXIETY *AE; NEUROSIS *AE; AGITATION *AE;

DIARRHEA *AE; ENCEPHALOPATHY *AE; EYE-DISEASE *AE; ELECTROLYTE-METAB.DISORDER *AE; GASTROENTEROPATHY *AE; GASTROENTEROPATHY *AE; GASTROENTEROPATHY *AE; VASCULAR-DISEASE *AE; EYE-DISEASE *AE; BODY-WEIGHT *AE; SLEEP *AE; MENTAL-DISORDER *AE; PSYCHOSIS *AE; GASTROENTEROPATHY *AE; PHENYTOIN *DI; FOSPHENYTOIN *DI; CARBAMAZEPINE *DI; DIAZEPAM *DI; CLONAZEPAM *DI; VALPROATE *DI; PHENOBARBITAL *DI; PRIMIDONE *DI; FELBAMATE *DI; GABAPENTIN *DI; LAMOTRIGINE *DI; LEVETIRACETAM *DI; OXCARBAZEPINE *DI; TIAGABINE *DI; TOPIRAMATE *DI; ZONISAMIDE *DI; PARACETAMOL *DI; ALLOPURINOL *DI; AMIODARONE *DI; CIMETIDINE *DI; CIPROFLOXACIN *DI; CLARITHROMYCIN *DI; ERYTHROMYCIN *DI; COLESTIPOL *DI; COLESTYRAMINE *DI; DANAZOL *DI; DILTIAZEM *DI; VERAPAMIL *DI; **FLUOXETINE** *DI; FLUVOXAMINE *DI; FOLATE *DI; HALOPERIDOL *DI; ISONIAZID *DI; METRONIDAZOLE *DI; LITHIUM-SALT *DI; **NEFAZODONE** *DI; PROPOXYPHENE *DI; PYRIDOXINE *DI; RIFAMPICIN *DI; SUCRALFATE *DI; SULFAMETHIZOLE *DI; SULFAPHENAZOLE *DI; TAMOXIFEN *DI; TICLOPIDINE *DI; TOLAZAMIDE *DI; TOLBUTAMIDE *DI; TRIMETHOPRIM *DI; GRAPEFRUIT-JUICE *FT; **COMB.** *FT; DI *FT

FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L148 ANSWER 9 OF 30 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-36152 DRUGU P S
TITLE: A pilot study on risperidone metabolism: the role of cytochromes P450 2D6 and 3A.
AUTHOR: Bork J A; Rogers T; Wedlund P J; de Leon J
CORPORATE SOURCE: Univ.Kentucky
LOCATION: Lexington, Ky., USA
SOURCE: J.Clin.Psychiatry (60, No. 7, 469-76, 1999) 2 Tab. 27 Ref.
CODEN: JCLPDE ISSN: 0160-6689
AVAIL. OF DOC.: University of Kentucky Mental Health Research Center at Eastern State Hospital, 627 West Fourth St., Lexington, KY 40508, U.S.A. (e-mail: jdeleon@pop.uky.edu). (J.D.L.).
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

A case series of 13 risperidone (RP) patients and an additional 20 RP patients from a case-control study with the CYP2D6 genotype were studied. CYP2D6 poor metabolizers (PM) or CYP2D6 deficient patients did not appear to tolerate RP, whereas CYP2D6 extensive metabolizers (EM) had fewer side effects. Adverse effects included severe akathisia, parkinsonian tremor, severe tardive dyskinesia, drowsiness, poor concentration and sedation. Drugs affecting CYP3A (inducers: carbamazepine (CB), mesoridazine (MS), phenytoin (PT) and paroxetine (PX), and inhibitors: nefazodone (NF) and fluoxetine (FX)) increased or decreased plasma RP levels.

SECTION HEADING: P Pharmacology
S Adverse Effects

CLASSIF. CODE: 8 Pharmacokinetics
32 Psychotropic
35 Adverse Reactions
59 CNS and Motor
66 Drug Interactions

CONTROLLED TERM:
P-450 *FT; ISOENZYME *FT; CASES *FT; IN-VIVO *FT; **COMB.** *FT; CYTOCHROME *FT

[01] RISPERIDONE *DM; RISPERIDONE *AE; RISPERIDONE *DI; SEVERE *AE; AKATHISIA *AE; TREMOR *AE; PARKINSONISM *AE; TARDIVE-DYSKINESIA *AE; DROWSINESS *AE; RESTLESSNESS *AE; MENTAL-DISORDER *AE; ENCEPHALOPATHY *AE; EXTRAPYRAMIDAL-DISORDER *AE; CARBAMAZEPINE *DI; MESORIDAZINE *DI; PHENYTOIN *DI; PAROXETINE *DI; **NEFAZODONE** *DI; **FLUOXETINE** *DI; OLANZAPINE *RC; HALOPERIDOL-DECANOATE *RC; RISPERIDO *RN; BLOOD-PLASMA *FT; CONC. *FT; CLEARANCE *FT; METABOLITE *FT; P.O. *FT; MICROSOME-DRUG-METAB. *FT; GENOTYPE *FT; PHARMACOKINETICS *FT; GENETICS *FT; NEUROLEPTICS *FT; PSYCHOSEDATIVES *FT; ANTISEROTONINS *FT; DOPAMINE-ANTAGONISTS *FT; DM *FT; AE *FT; DI *FT

CAS REGISTRY NO.: 106266-06-2

[02] CARBAMAZEPINE *DI; RISPERIDONE *DI; CARBAMAZE *RN; ANTIMANICS *FT; ANTICONVULSANTS *FT; DI *FT

CAS REGISTRY NO.: 90-89-1

[03] MESORIDAZINE *DI; MESORIDAZINE *AE; TREMOR *AE; AKATHISIA *AE; RISPERIDONE *DI; MESORIDAZ *RN; DOPAMINE-ANTAGONISTS *FT; PSYCHOSEDATIVES *FT; NEUROLEPTICS *FT; DI *FT; AE *FT

CAS REGISTRY NO.: 5588-33-0

[04] PHENYTOIN *DI; RISPERIDONE *DI; PHENYTOIN *RN; ANTICONVULSANTS *FT; DI *FT

CAS REGISTRY NO.: 57-41-0

[05] PAROXETINE *DI; RISPERIDONE *DI; PAROXETIN *RN; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; DI *FT

CAS REGISTRY NO.: 61869-08-7

[06] **NEFAZODONE** *DI; SEVERE *AE; AKATHISIA *AE; PARKINSONISM *AE; ENCEPHALOPATHY *AE; EXTRAPYRAMIDAL-DISORDER *AE; RISPERIDONE *DI; NEFAZODON *RN; ANTIDEPRESSANTS *FT; PSYCHOSTIMULANTS *FT; DI *FT

CAS REGISTRY NO.: 83366-66-9

[07] **FLUOXETINE** *DI; RISPERIDONE *DI; FLUOXETIN *RN; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; DI *FT

CAS REGISTRY NO.: 54910-89-3

[08] HYDROXYRISPERIDONE-9 *DM; HORISPER9 *RN; CONC. *FT; METABOLITE *FT; BIOSYNTH. *FT; DM *FT

FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L148 ANSWER 10 OF 30 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1997-06398 DRUGU P T S
TITLE: Pharmacokinetic and pharmacodynamic drug interactions with polypharmacotherapy of treatment-resistant affective and obsessive-compulsive disorders.
AUTHOR: Carson S W
CORPORATE SOURCE: Univ.North-Carolina
LOCATION: Chapel Hill, N.C., USA
SOURCE: Psychopharmacol.Bull. (32, No. 4, 555-68, 1997) 1 Tab. 56 Ref.
CODEN: PSYBB9 ISSN: 0048-5764
AVAIL. OF DOC.: School of Pharmacy, Beard Hall, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599-7360, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

The pharmacokinetic and pharmacodynamic interactions that may occur with the polypharmacotherapy of obsessive-compulsive disorders (OCD) are reviewed, with reference to the use of antidepressants, mood stabilizers and neuroleptics and to the prediction of drug interactions.

SECTION HEADING: P Pharmacology

T Therapeutics
S Adverse Effects

CLASSIF. CODE: 8 Pharmacokinetics
33 Respiratory
35 Adverse Reactions
66 Drug Interactions
69 Reviews

CONTROLLED TERM:
OBSESSIVE *TR; COMPULSIVE *TR; NEUROSIS *TR; MENTAL-DISORDER *TR; REVIEW *FT; CASES *FT; IN-VIVO *FT; ANTIDEPRESSANT *FT; NEUROLEPTIC *FT; PSYCHOSTIMULANT *FT; PSYCHOSEDATIVE *FT
[01] MAIN-TOPIC *FT; **COMB.** *FT; TR *FT; DM *FT; DI *FT
[02] QUINIDINE *DM; PAROXETINE *DM; NORFLUOXETINE *DM; **FLUOXETINE** *DM; SERTRALINE *DM; THIORIDAZINE *DM; PAROXETINE *DM; CLOMIPRAMINE *DM; DESIPRAMINE *DM; CITALOPRAM *DM; FLUVOXAMINE *DM; CP-53261 *DM; QUINIDINE *DI; PAROXETINE *DI; NORFLUOXETINE *DI; **FLUOXETINE** *DI; SERTRALINE *DI; THIORIDAZINE *DI; PAROXETINE *DI; CLOMIPRAMINE *DI; DESIPRAMINE *DI; CITALOPRAM *DI; FLUVOXAMINE *DI; CP-53261 *DI; WARFARIN *DI; DIGOXIN *DI; WARFARIN *DM; DIGOXIN *DM; **NEFAZODONE** *DM; TRIAZOLAM *DM; ALPRAZOLAM *DM; LORAZEPAM *DM; IMIPRAMINE *DM; HALOPERIDOL *DM; CARBAMAZEPINE *DM; TIOTIXENE *DM; PERPHENAZINE *DM; TR *FT; DM *FT; DI *FT; AE *FT
[03] **NEFAZODONE** *DI; TRIAZOLAM *DI; ALPRAZOLAM *DI; LORAZEPAM *DI; IMIPRAMINE *DI; HALOPERIDOL *DI; CARBAMAZEPINE *DI; TIOTIXENE *DI; PERPHENAZINE *DI; CLOZAPINE *DI; CLOZAPINE *DM; BUPROPION *DM; VALPROATE *DM; BUPROPION *DI; VALPROATE *DI; LITHIUM-SALT *TR; BUSPIRONE *TR; LITHIUM-SALT *DI; BUSPIRONE *DI; QUINIDINE *TR; PAROXETINE *TR; NORFLUOXETINE *TR; **FLUOXETINE** *TR; SERTRALINE *TR; THIORIDAZINE *TR; PAROXETINE *TR; CLOMIPRAMINE *TR; DESIPRAMINE *TR; CITALOPRAM *TR; FLUVOXAMINE *TR; CP-53261 *TR; WARFARIN *TR; DIGOXIN *TR; WARFARIN *TR; DIGOXIN *TR; **NEFAZODONE** *TR; TRIAZOLAM *TR; ALPRAZOLAM *TR; LORAZEPAM *TR; IMIPRAMINE *TR; HALOPERIDOL *TR; CARBAMAZEPINE *TR; TIOTIXENE *TR; PERPHENAZINE *TR; LITHIUM-SALT *AE; BUSPIRONE *AE; DI *FT; DM *FT; TR *FT; AE *FT
[04] PAROXETINE *AE; NORFLUOXETINE *AE; **FLUOXETINE** *AE; SERTRALINE *AE; THIORIDAZINE *AE; PAROXETINE *AE; CLOMIPRAMINE *AE; DESIPRAMINE *AE; CITALOPRAM *AE; FLUVOXAMINE *AE; TRAZODONE *AE; TRANYLCYPROMINE *DI; TRANYLCYPROMINE *TR; TRANYLCYPROMINE *AE; VENLAFAXINE *TR; VENLAFAXINE *AE; VENLAFAXINE *DI; PHENELZINE *TR; PHENELZINE *DI; PHENELZINE *AE; METHYSERGIDE *TR; CYPROHEPTADINE *TR; PROPRANOLOL *TR; ISOCARBOXAZID *TR; PHENYTOIN *DM; PHENOBARBITAL *DM; RIFAMPICIN *DM; ISONIAZID *DM; PHENYTOIN *DI; PHENOBARBITAL *DI; RIFAMPICIN *DI; ISONIAZID *DI; AE *FT
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L148 ANSWER 11 OF 30 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1998-11856 DRUGU P
TITLE: Clinical implications of genetic polymorphisms and drug interactions mediated by cytochrome P-450 enzymes.
AUTHOR: Touw D J
CORPORATE SOURCE: Univ.Vrije
LOCATION: Amsterdam, Neth.
SOURCE: Drug Metab.Drug Interact. (14, No. 2, 55-82, 1997) 1 Fig. 6 Tab. 89 Ref.
CODEN: DMDIEQ ISSN: 0334-2190

AVAIL. OF DOC.: Department of Pharmacy, University Hospital Vrije Universiteit, P.O. Box 7057, J007 MB Amsterdam, The Netherlands.
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

The clinical implications of drug interactions mediated by cytochrome P-450 enzymes are reviewed with respect to genetic polymorphism, gender, age and racial differences in hepatic metabolism, use of drug-drug interactions to lower dosages, and the consequences of genetic polymorphism for drug development. The relevant cytochromes involved in drug metabolism are 1A2, 2C8, 2C9/10, 2C19, 2C6, 2E1, 3A4.

SECTION HEADING: P Pharmacology

CLASSIF. CODE: **66 Drug Interactions**

CONTROLLED TERM:
IN-VIVO *FT; **COMB.** *FT; P-450 *FT; ISOENZYME *FT; CYTOCHROME *FT
[01] DI *FT
[02] FLUVOXAMINE *DI; CAFFEINE *DI; MOCLOBEMIDE *DI; DILTIAZEM *DI; ENOXACIN *DI; CIPROFLOXACIN *DI; PEFLOXACIN *DI; OMEPRAZOLE *DI; RIFAMPICIN *DI; **FLUOXETINE** *DI; PROGUANIL *DI; PHENOBARBITONE *DI; QUINIDINE *DI; PAROXETENE *DI; SERTRALINE *DI; CIMETIDINE *DI; DISULFRAM *DI; ISONIAZID *DI; ETHYL-ALCOHOL *DI; CIMETIDINE *DI; KETOCONAZOLE *DI; ITRACONAZOLE *DI; FLUCONAZOLE *DI; **NEFAZODONE** *DI; DILTIAZEM *DI; ERYTHROMYCIN *DI; CARBAMAZEPINE *DI; PENTOBARBITAL *DI; PHENYTOIN *DI; DI *FT
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L148 ANSWER 12 OF 30 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1996-48975 DRUGU T P S
TITLE: Clinically significant interactions of psychotropic agents with antipsychotic drugs.
AUTHOR: Meyer M C; Baldessarini R J; Goff D C; Centorrino F
CORPORATE SOURCE: Univ.Harvard
LOCATION: Boston; Belmont, Mass., USA
SOURCE: Drug Safety (15, No. 5, 335-46, 1996) 1 Tab. 200 Ref. ISSN: 0114-5916
AVAIL. OF DOC.: Division of Child Psychiatry, Department of Psychiatry, Massachusetts General Hospital, ACC-725, Boston, MA 02114, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

The clinically significant interactions of typical and atypical psychotropic and antipsychotic drugs are reviewed, with reference to anticholinergics such as benzatropine, amantadine and trihexyphenidyl; antidepressants such as amitriptyline, doxepin, imipramine, protriptyline, fluoxetine, trazodone and nefazodone; anticonvulsants such as phenytoin, valproate, gabapentin, felbamate, lamotrigine and carbamazepine; Li salts and anxiolytics such as buspirone, lorazepam and clonazepam.

SECTION HEADING: T Therapeutics
P Pharmacology
S Adverse Effects

CLASSIF. CODE:
8 Pharmacokinetics
32 Psychotropic
35 Adverse Reactions
59 CNS and Motor
66 Drug Interactions
69 Reviews

CONTROLLED TERM:

PSYCHOSIS *TR; MENTAL-DISORDER *TR; **COMB**. *FT; CASES *FT; IN-VIVO *FT; REVIEW *FT; NEUROLEPTIC *FT; ANTIDEPRESSANT *FT; ANTICONVULSANT *FT; PARASYMPATHOLYTIC *FT; TRANQUILIZER *FT; PSYCHOSEDATIVE *FT; PSYCHOSTIMULANT *FT; PSYCHOSEDATIVE *FT

[01] MAIN-TOPIC *FT; NEUROLEPTICS *FT; ANTIDEPRESSANTS *FT; ANTICONVULSANTS *FT; TRANQUILIZERS *FT; PSYCHOSEDATIVES *FT; PSYCHOSTIMULANTS *FT; PSYCHOSEDATIVES *FT; DI *FT

[02] CLOZAPINE *DI; HALOPERIDOL *DI; OLANZAPINE *DI; IMIPRAMINE *DI; FLUVOXAMINE *DI; CHLORPROMAZINE *DI; FLUPHENAZINE *DI; PERPHENAZINE *DI; RISPERIDONE *DI; THIORIDAZINE *DI; TRIFLUPERIDOL *DI; ZUCLOPENTHIXOL *DI; AMITRIPTYLINE *DI; CLOMIPRAMINE *DI; DESIPRAMINE *DI; MAPROTILINE *DI; **FLUOXETINE** *DI; PAROXETINE *DI; SERTRALINE *DI; TRAZODONE *DI; PHENOTHIAZINE *DI; **NEFAZODONE** *DI; VENLAFEXINE *DI; RISPERIDONE *DI; **FLUOXETINE** *DI; PAROXETINE *DI; PIMOZIDE *DI; CARBAMAZEPINE *DI; VALPROATE *DI; FELBAMATE *DI; LAMOTRIGINE *DI; BENZATROPINE *DI; AMANTADINE *DI; TRIHEXYPHENIDYL *DI; AMITRIPTYLINE *DI; DOXEPIN *DI; IMIPRAMINE *DI; PROTRIPTYLINE *DI; **FLUOXETINE** *DI; TRAZODONE *DI; **NEFAZODONE** *DI; PHENYTOIN *DI; VALPROATE *DI; GABAPENTIN *DI; CARBAMAZEPINE *DI; LITHIUM-SALT *DI; BUSPIRONE *DI; LORAZEPAM *DI; CLONAZEPAM *DI; PROPRANOLOL *DI; DI *FT

[03] CLOZAPINE *DM; HALOPERIDOL *DM; OLANZAPINE *DM; IMIPRAMINE *DM; FLUVOXAMINE *DM; CHLORPROMAZINE *DM; FLUPHENAZINE *DM; PERPHENAZINE *DM; RISPERIDONE *DM; THIORIDAZINE *DM; TRIFLUPERIDOL *DM; ZUCLOPENTHIXOL *DM; AMITRIPTYLINE *DM; CLOMIPRAMINE *DM; DESIPRAMINE *DM; MAPROTILINE *DM; **FLUOXETINE** *DM; PAROXETINE *DM; SERTRALINE *DM; TRAZODONE *DM; PHENOTHIAZINE *DM; **NEFAZODONE** *DM; VENLAFEXINE *DM; RISPERIDONE *DM; **FLUOXETINE** *DM; PAROXETINE *DM; PIMOZIDE *DM; CARBAMAZEPINE *DM; VALPROATE *DM; FELBAMATE *DM; LAMOTRIGINE *DM; BENZATROPINE *DM; AMANTADINE *DM; TRIHEXYPHENIDYL *DM; AMITRIPTYLINE *DM; DOXEPIN *DM; IMIPRAMINE *DM; PROTRIPTYLINE *DM; **FLUOXETINE** *DM; TRAZODONE *DM; **NEFAZODONE** *DM; PHENYTOIN *DM; VALPROATE *DM; GABAPENTIN *DM; CARBAMAZEPINE *DM; LITHIUM-SALT *DM; BUSPIRONE *DM; LORAZEPAM *DM; CLONAZEPAM *DM; PROPRANOLOL *DM; DM *FT

[04] CLOZAPINE *TR; HALOPERIDOL *TR; OLANZAPINE *TR; IMIPRAMINE *TR; FLUVOXAMINE *TR; CHLORPROMAZINE *TR; FLUPHENAZINE *TR; PERPHENAZINE *TR; RISPERIDONE *TR; THIORIDAZINE *TR; TRIFLUPERIDOL *TR; ZUCLOPENTHIXOL *TR; AMITRIPTYLINE *TR; CLOMIPRAMINE *TR; DESIPRAMINE *TR; MAPROTILINE *TR; **FLUOXETINE** *TR; PAROXETINE *TR; SERTRALINE *TR; TRAZODONE *TR; PHENOTHIAZINE *TR; **NEFAZODONE** *TR; VENLAFEXINE *TR; RISPERIDONE *TR; **FLUOXETINE** *TR; PAROXETINE *TR; PIMOZIDE *TR; CARBAMAZEPINE *TR; VALPROATE *TR; FELBAMATE *TR; LAMOTRIGINE *TR; BENZATROPINE *TR; AMANTADINE *TR; TRIHEXYPHENIDYL *TR; AMITRIPTYLINE *TR; DOXEPIN *TR; IMIPRAMINE *TR; PROTRIPTYLINE *TR; **FLUOXETINE** *TR; TRAZODONE *TR; **NEFAZODONE** *TR; PHENYTOIN *TR; VALPROATE *TR; GABAPENTIN *TR;

CARBAMAZEPINE *TR; LITHIUM-SALT *TR; BUSPIRONE *TR; LORAZEPAM *TR; CLONAZEPAM *TR; TR *FT

[05] CLOZAPINE *AE; HALOPERIDOL *AE; OLANZAPINE *AE; IMIPRAMINE *AE; FLUVOXAMINE *AE; CHLORPROMAZINE *AE; FLUPHENAZINE *AE; PERPHENAZINE *AE; RISPERIDONE *AE; THIORIDAZINE *AE; TRIFLUPERIDOL *AE; ZUCLOPENTHIXOL *AE; AMITRIPTYLINE *AE; CLOMIPRAMINE *AE; DESIPRAMINE *AE; MAPROTILINE *AE; **FLUOXETINE** *AE; PAROXETINE *AE; SERTRALINE *AE; TRAZODONE *AE; PHENOTHIAZINE *AE; **NEFAZODONE** *AE; VENLAFEXINE *AE; RISPERIDONE *AE; **FLUOXETINE** *AE; PAROXETINE *AE; PIMOZIDE *AE; CARBAMAZEPINE *AE; VALPROATE *AE; FELBAMATE *AE; LAMOTRIGINE *AE; BENZATROPINE *AE; AMANTADINE *AE; TRIHEXYPHENIDYL *AE; AMITRIPTYLINE *AE; DOXEPIN *AE; IMIPRAMINE *AE; PROTRIPTYLINE *AE; **FLUOXETINE** *AE; TRAZODONE *AE; **NEFAZODONE** *AE; PHENYTOIN *AE; VALPROATE *AE; GABAPENTIN *AE; CARBAMAZEPINE *AE; LITHIUM-SALT *AE; BUSPIRONE *AE; LORAZEPAM *AE; CLONAZEPAM *AE; AE *FT

FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L148 ANSWER 13 OF 30 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1996-16477 DRUGU P
TITLE: Interaction of nefazodone (N) and fluoxetine (F).
AUTHOR: Marino M R; Langenbacher K M; Uderman H D
CORPORATE SOURCE: Bristol-Squibb
LOCATION: Princeton, N.J., USA
SOURCE: Clin.Pharmacol.Ther. (59, No. 2, 180, 1996) 1 Tab.
CODEN: CLPTAT ISSN: 0009-9236
AVAIL. OF DOC.: Bristol-Myers Squibb Pharmaceutical Research Institute and Clinical Pharmacology Unit, The Medical Center at Princeton, Princeton, NJ, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

Both nefazodone (NE) and fluoxetine (FL) were competitive inhibitors of ex-vivo platelet serotonin uptake however their effects were not syngeristic in a randomized, double-blind, parallel group study in healthy male subjects. NE did not alter the pharmacokinetics of FL or norFL. FL pretreatment or coadministration had no effect on the levels of NE or hydroxyne but increased mecoprop (mCPP) and dione. The increased level of mCPP was probably due to the inhibition CYP2D6 by FL, thereby, inhibiting the hydroxylation of mCPP. (conference abstract).

SECTION HEADING: P Pharmacology

CLASSIF. CODE: 8 Pharmacokinetics
60 Autonomic
66 Drug Interactions

CONTROLLED TERM:
BLOOD-PLASMA *FT; CLEARANCE *FT; CONC. *FT; PHARMACOKINETICS *FT
[01] MECOPROP *DM; MECOPROP *RN; BIOSYNTH. *FT; DM *FT; HERBICIDES *FT
CAS REGISTRY NO.: 7085-19-0
[02] **HYDROXYNEFAZODONE** *DM; HONEFAZOD *RN; BIOSYNTH. *FT; DM *FT
[03] NORFLUOXETINE *DM; NORFLUOXE *RN; ANTIDEPRESSANTS *FT; BIOSYNTH. *FT; DM *FT; PSYCHOSTIMULANTS *FT
CAS REGISTRY NO.: 83891-03-6

[04] **FLUOXETINE** *DI; **FLUOXETINE** *DM; FLUOXETIN *RN; **NEFAZODONE** *DI; ANTIDEPRESSANTS *FT; BLIND-TEST *FT; **COMB.** *FT; COMPETITIVE *FT; DI *FT; DM *FT; DOUBLE *FT; EC-1.14.14.1 *FT; FLAVOPROTEIN-LINKED-MONOOXYGENASE *FT; HUMAN *FT; IN-VIVO *FT; INHIBITION *FT; METABOLITE *FT; PLATELET *FT; PSYCHOSTIMULANTS *FT; RANDOM *FT; SEROTONIN *FT

CAS REGISTRY NO.: 54910-89-3

[05] **NEFAZODONE** *DI; NEFAZODON *RN; **FLUOXETINE** *DI; ANTIDEPRESSANTS *FT; BLIND-TEST *FT; **COMB.** *FT; COMPETITIVE *FT; DI *FT; DOUBLE *FT; EC-1.14.14.1 *FT; FLAVOPROTEIN-LINKED-MONOOXYGENASE *FT; HUMAN *FT; IN-VIVO *FT; INHIBITION *FT; METABOLITE *FT; PLATELET *FT; PSYCHOSTIMULANTS *FT; RANDOM *FT; SEROTONIN *FT

CAS REGISTRY NO.: 83366-66-9
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L148 ANSWER 14 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:963693 CAPLUS
DOCUMENT NUMBER: 138:29139
TITLE: Pyridoxal in combination with serotonin re-uptake inhibitor for the treatment of hot flashes
INVENTOR(S): Coelingh Bennink, Herman Jan Tijmen; Van Der Linden, Rene Frank
PATENT ASSIGNEE(S): Pantarhei Bioscience B.V., Neth.
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1266659	A1	20021218	EP 2001-202230	20010611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
WO 2002100404	A2	20021219	WO 2002-NL382	20020611
WO 2002100404	A3	20030313		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2001-202230 A 20010611

AB The present invention is concerned with formulations for use in a method of suppressing hot flushes, esp. hot flashes in hypo-estrogenic females and androgen-deprived males. More particularly the invention relates to a pharmaceutical formulation for use in a method of suppressing hot flashes, said method comprising the administration of the formulation so as to provide on a daily basis a combination of a serotonin re-uptake inhibitor in an amt. which is equiv. to <100 mg trazodone and vitamin B6 component, in an amt. effective to to reduce the incidence and/or intensity of hot flashes. Another aspect of the invention relates to pharmaceutical

formulations comprising a combination of serotonin re-uptake inhibitor at 0.6-45 mg, preferably 0.6-24 mg trazodone and 0.005-5 mM vitamin B6 component, and addnl. comprising an acceptable excipient. A clin. study is conducted with 12 peri-menopausal women experiencing at least 40-50 hot flashes/wk. During the study, the medication is orally administered once a day. The visual aspects of the medication used are always the same. The no. of hot flashes experienced per day, decreases substantially over time, indicating that 20 mg fluoxetine-HCl is efficacious in suppressing hot flashes.

IT **54910-89-3, Fluoxetine 56296-78-7, Fluoxetine** hydrochloride **83366-66-9, Nefazodone**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pyridoxal in **combination** with serotonin re-uptake inhibitor for treatment of hot flashes)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L148 ANSWER 15 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:434867 CAPLUS
DOCUMENT NUMBER: 135:29158
TITLE: The combination of a serotonin reuptake inhibitor and irindalone for the treatment of depression and other affective disorders
INVENTOR(S): Bogeso, Klaus Peter; Cremers, Thomas Ivo Franciscus Hubert
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001041766	A1	20010614	WO 2000-DK667	20001204
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002103249	A1	20020801	US 2000-731411	20001206

PRIORITY APPLN. INFO.: US 1999-169245P P 19991206

AB The invention discloses the use of a combination of irindalone and a serotonin reuptake inhibitor, or any other compd. which causes an elevation in the level of extracellular serotonin, for the treatment of depression and other affective disorders.

IT **54910-89-3, Fluoxetine 83366-66-9, Nefazodone**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(irindalone-serotonin reuptake inhibitor **combination** for treatment of depression and other affective disorders)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L148 ANSWER 16 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:98327 CAPLUS
DOCUMENT NUMBER: 132:146650
TITLE: Treating depression with a combination of a serotonin uptake inhibitor, a 5-HT1A presynaptic antagonist, and a 5-HT1A agonist
INVENTOR(S): Depoortere, Henri
PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006160	A1	20000210	WO 1999-FR1825	19990726
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2781671	A1	20000204	FR 1998-9603	19980728
AU 9949167	A1	20000221	AU 1999-49167	19990726

PRIORITY APPLN. INFO.: FR 1998-9603 A 19980728
WO 1999-FR1825 W 19990726

AB Pharmaceutical compns. are provided which contain a serotonin uptake inhibitor (e.g. fluoxetine), a 5-HT1A presynaptic antagonist (e.g. pindolol), and a 5-HT1A agonist (e.g. buspirone) as a combination product for simultaneous, sep., or prolonged use for treating various forms of depression.

IT **54910-89-3, Fluoxetine 83366-66-9, Nefazodone**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(serotonin uptake inhibitor-5-HT1A presynaptic antagonist-5-HT1A agonist **combination** for treatment of depression)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L148 ANSWER 17 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:33506 CAPLUS
DOCUMENT NUMBER: 132:73655
TITLE: Agent with antidepressive effect
INVENTOR(S): Maj, Jerzy
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: Ger. Offen., 4 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19830201	A1	20000113	DE 1998-19830201	19980707
CA 2301899	AA	20000210	CA 1998-2301899	19980727

WO 2000006162	A1	20000210	WO 1998-EP4691	19980727
W: CA, US				
AU 9950303	A1	20000201	AU 1999-50303	19990701
AU 762128	B2	20030619		
CA 2336833	AA	20000120	CA 1999-2336833	19990702
WO 2000002542	A2	20000120	WO 1999-EP4595	19990702
WO 2000002542	A3	20000622		
W: AU, BG, BR, CA, CN, CZ, EE, HU, ID, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
BR 9911768	A	20010403	BR 1999-11768	19990702
EP 1093369	A2	20010425	EP 1999-934560	19990702
EP 1093369	B1	20021127		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EE 200100014	A	20020617	EE 2001-14	19990702
JP 2002520273	T2	20020709	JP 2000-558802	19990702
AT 228365	E	20021215	AT 1999-934560	19990702
ES 2183583	T3	20030316	ES 1999-934560	19990702
NZ 509729	A	20030630	NZ 1999-509729	19990702
US 6255329	B1	20010703	US 1999-348591	19990706
BG 105112	A	20011031	BG 2001-105112	20010103
ZA 2001000090	A	20020404	ZA 2001-90	20010104
NO 2001000064	A	20010302	NO 2001-64	20010105

PRIORITY APPLN. INFO.: DE 1998-19830201 A 19980707
WO 1998-EP4691 A 19980727
WO 1999-EP4595 W 19990702

AB 2-Amino-4,5,6,7-tetrahydro-6-propylaminobenzothiazole (pramipexole), (+)- or (-)-pramipexole, or a salt thereof can be used synergistically in combination with another antidepressant for improved treatment of depression (no data).

IT **54910-89-3, Fluoxetine 83366-66-9, Nefazodone**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**combination** with pramipexole; agent with antidepressive effect)

L148 ANSWER 18 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:365808 CAPLUS
DOCUMENT NUMBER: 125:19076
TITLE: Combination of an opioid antagonist and a selective serotonin reuptake inhibitor for treatment of alcoholism and alcohol dependence
INVENTOR(S): Cook, Leonard
PATENT ASSIGNEE(S): Du Pont Merck Pharmaceutical Company, USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9609047	A1	19960328	WO 1995-US10987	19950907
W: AU, BR, CA, CN, CZ, EE, FI, HU, JP, KR, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, UA, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9534199	A1	19960409	AU 1995-34199	19950907

EP 782445 A1 19970709 EP 1995-931014 19950907
EP 782445 B1 20020313
R: AT, BE, DE, DK, FR, GB, IE, IT
AT 214276 E 20020315 AT 1995-931014 19950907
ZA 9507891 A 19970319 ZA 1995-7891 19950919
US 5958962 A 19990928 US 1995-542747 19951013
PRIORITY APPLN. INFO.: US 1994-308859 A 19940919
WO 1995-US10987 W 19950907

AB The invention relates to a method of treating alcoholism and alc. dependence in a mammal comprising administering to the mammal a therapeutically effective amt. of a synergistic combination of: (i) at least one opioid antagonist, and (ii) at least one selective serotonin reuptake inhibitor. The invention also relates to compns. and kits contg. the same.

IT **54910-89-3, Fluoxetine 83366-66-9, Nefazodone**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**combination** of an opioid antagonist and a selective serotonin reuptake inhibitor for treatment of alcoholism and alc. dependence)

L148 ANSWER 19 OF 30 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003251236 EMBASE
TITLE: St. John's wort: A systematic review of adverse effects and drug **interactions** for the consultation psychiatrist.
AUTHOR: Hammerness P.; Basch E.; Ulbricht C.; Barrette E.-P.; Foppa I.; Basch S.; Bent S.; Boon H.; Ernst E.
CORPORATE SOURCE: Dr. C. Ulbricht, Nat. Standard Research Collaboration, P.O. Box 390709, Cambridge, MA 02139-0008, United States. kate@naturalstandard.com
SOURCE: Psychosomatics, (2003) 44/4 (271-282).
Refs: 129
ISSN: 0033-3182 CODEN: PSYCBC
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
St. John's wort is an herb commonly used in Europe for decades and more recently the topic of scientific investigation in this country. St. John's wort has been found more effective than placebo and equally as effective as tricyclic antidepressants in the short-term management of mild-to-moderate depression. Comparisons to selective serotonin reuptake inhibitors have provided equivocal data. While it is generally well tolerated in clinical use, there is accumulating evidence of significant interactions with drugs. This evidence-based presentation of the literature includes a brief description of pharmacodynamics and clinical applications, followed by a systematic review of adverse effects, toxicity, and drug interactions.

CONTROLLED TERM: Medical Descriptors:
*Hypericum perforatum
consultation

psychiatrist
evidence based medicine
drug mechanism
drug indication
pharmacodynamics
mood disorder: DT, drug therapy
anxiety disorder: DT, drug therapy
Europe
depression: DT, drug therapy
pregnancy
fatigue: SI, side effect
sedation
side effect: SI, side effect
restlessness: SI, side effect
vertigo: SI, side effect
headache: SI, side effect
xerostomia: SI, side effect
allergy: SI, side effect
skin disease: SI, side effect
skin manifestation: SI, side effect
rash: SI, side effect
pruritus: SI, side effect
phototoxicity: SI, side effect
alopecia: SI, side effect
neurologic disease: SI, side effect
central nervous system disease: SI, side effect
neuropathy: SI, side effect
mental disease: SI, side effect
insomnia: SI, side effect
nervousness
mania: SI, side effect
serotonin syndrome: SI, side effect
flushing
diaphoresis
hypertension: SI, side effect
disorientation: SI, side effect
dyspnea: SI, side effect
tremor: SI, side effect
psychosis: SI, side effect
cardiovascular disease: SI, side effect
delirium: SI, side effect
heart muscle conduction disturbance: SI, side effect
tachycardia: SI, side effect
gastrointestinal disease: SI, side effect
dyspepsia: SI, side effect
anorexia: SI, side effect
diarrhea: SI, side effect
nausea: SI, side effect
constipation: SI, side effect
urogenital tract disease: SI, side effect
anorgasmia: SI, side effect
sexual dysfunction: SI, side effect
mood disorder: SI, side effect
libido disorder: SI, side effect
orgasm disorder: SI, side effect
erectile dysfunction: SI, side effect
spermatozoon motility
drug metabolism
breakthrough bleeding: SI, side effect
thromboembolism: SI, side effect
hyperreflexia: SI, side effect
involuntary movement
vomiting: SI, side effect

confusion: SI, side effect
irritability
hypomania: SI, side effect
food drug interaction
agitation
human
nonhuman
clinical trial
review
Drug Descriptors:
*Hypericum perforatum extract: AE, adverse drug reaction
*Hypericum perforatum extract: CT, clinical trial
*Hypericum perforatum extract: CB, drug combination
*Hypericum perforatum extract: CM, drug comparison
*Hypericum perforatum extract: DO, drug dose
***Hypericum perforatum extract: IT, drug interaction**
*Hypericum perforatum extract: DT, drug therapy
*Hypericum perforatum extract: TO, drug toxicity
*Hypericum perforatum extract: PK, pharmacokinetics
*Hypericum perforatum extract: PD, pharmacology
*Hypericum perforatum extract: IV, intravenous drug administration
*Hypericum perforatum extract: PO, oral drug administration
*hypericin: AE, adverse drug reaction
*hypericin: CT, clinical trial
*hypericin: CB, drug combination
*hypericin: CM, drug comparison
*hypericin: DO, drug dose
***hypericin: IT, drug interaction**
*hypericin: DT, drug therapy
*hypericin: TO, drug toxicity
*hypericin: PK, pharmacokinetics
*hypericin: PD, pharmacology
*hypericin: IV, intravenous drug administration
*hypericin: PO, oral drug administration
placebo
tricyclic antidepressant agent: CT, clinical trial
tricyclic antidepressant agent: CB, drug combination
tricyclic antidepressant agent: CM, drug comparison
tricyclic antidepressant agent: CR, drug concentration
tricyclic antidepressant agent: IT, drug interaction
tricyclic antidepressant agent: DT, drug therapy
tricyclic antidepressant agent: PK, pharmacokinetics
sertraline: AE, adverse drug reaction
sertraline: CT, clinical trial
sertraline: CB, drug combination
sertraline: CM, drug comparison
sertraline: IT, drug interaction
sertraline: DT, drug therapy
cytochrome P450
carbamazepine: CT, clinical trial
carbamazepine: CR, drug concentration
carbamazepine: IT, drug interaction
carbamazepine: PK, pharmacokinetics
cyclosporin: CR, drug concentration
cyclosporin: IT, drug interaction
cyclosporin: PK, pharmacokinetics
ethinylestradiol: AE, adverse drug reaction
ethinylestradiol: CB, drug combination
ethinylestradiol: IT, drug interaction
ethinylestradiol: PK, pharmacokinetics
desogestrel: AE, adverse drug reaction

desogestrel: CB, drug combination
desogestrel: IT, drug interaction
desogestrel: PK, pharmacokinetics
oral contraceptive agent: AE, adverse drug reaction
oral contraceptive agent: CB, drug combination
oral contraceptive agent: IT, drug interaction
oral contraceptive agent: PK, pharmacokinetics
hydroxymethylglutaryl coenzyme A reductase inhibitor: CB, drug combination
hydroxymethylglutaryl coenzyme A reductase inhibitor: CR, drug concentration
hydroxymethylglutaryl coenzyme A reductase inhibitor: IT, drug interaction
hydroxymethylglutaryl coenzyme A reductase inhibitor: PK, pharmacokinetics
simvastatin: CB, drug combination
simvastatin: CR, drug concentration
simvastatin: IT, drug interaction
simvastatin: PK, pharmacokinetics
drug metabolite: CB, drug combination
drug metabolite: CR, drug concentration
drug metabolite: IT, drug interaction
drug metabolite: PK, pharmacokinetics
midazolam: CR, drug concentration
midazolam: IT, drug interaction
midazolam: PK, pharmacokinetics
nifedipine: CR, drug concentration
nifedipine: IT, drug interaction
nifedipine: PK, pharmacokinetics
proteinase inhibitor: CR, drug concentration
proteinase inhibitor: IT, drug interaction
proteinase inhibitor: PK, pharmacokinetics
RNA directed DNA polymerase inhibitor: CR, drug concentration
RNA directed DNA polymerase inhibitor: IT, drug interaction
RNA directed DNA polymerase inhibitor: PK, pharmacokinetics
nevirapine: IT, drug interaction
nevirapine: PK, pharmacokinetics
nevirapine: PO, oral drug administration
indinavir: CT, clinical trial
indinavir: CR, drug concentration
indinavir: IT, drug interaction
indinavir: PK, pharmacokinetics
irinotecan: CT, clinical trial
irinotecan: CB, drug combination
irinotecan: IT, drug interaction
irinotecan: PK, pharmacokinetics
irinotecan: IV, intravenous drug administration
theophylline: CR, drug concentration
theophylline: IT, drug interaction
theophylline: PK, pharmacokinetics
warfarin: AE, adverse drug reaction
warfarin: CB, drug combination
warfarin: DO, drug dose
warfarin: IT, drug interaction
warfarin: PK, pharmacokinetics
amitriptyline: CT, clinical trial
amitriptyline: CB, drug combination
amitriptyline: CR, drug concentration
amitriptyline: IT, drug interaction
amitriptyline: PK, pharmacokinetics
paroxetine: AE, adverse drug reaction

paroxetine: CB, drug combination
paroxetine: DO, drug dose
paroxetine: IT, drug interaction
paroxetine: DT, drug therapy
nefazodone: AE, adverse drug reaction
nefazodone: CB, drug combination
nefazodone: IT, drug interaction
nefazodone: DT, drug therapy
Ginkgo biloba extract: AE, adverse drug reaction
Ginkgo biloba extract: CB, drug combination
Ginkgo biloba extract: IT, drug interaction
Ginkgo biloba extract: DT, drug therapy
fluoxetine: AE, adverse drug reaction
fluoxetine: CB, drug combination
fluoxetine: IT, drug interaction
fluoxetine: DT, drug therapy
buspirone: AE, adverse drug reaction
buspirone: CB, drug combination
buspirone: IT, drug interaction
buspirone: DT, drug therapy
unindexed drug

CAS REGISTRY NO.: (hypericin) 548-04-9; (sertraline) 79617-96-2; (cytochrome P450) 9035-51-2; (carbamazepine) 298-46-4, 8047-84-5; (cyclosporin) 79217-60-0; (ethinylestradiol) 57-63-6; (desogestrel) 54024-22-5; (simvastatin) 79902-63-9; (midazolam) 59467-70-8; (nifedipine) 21829-25-4; (proteinase inhibitor) 37205-61-1; (nevirapine) 129618-40-2; (indinavir) 150378-17-9, 157810-81-6, 180683-37-8; (irinotecan) 100286-90-6; (theophylline) 58-55-9, 5967-84-0, 8055-07-0, 8061-56-1, 99007-19-9; (warfarin) 129-06-6, 2610-86-8, 3324-63-8, 5543-58-8, 81-81-2; (amitriptyline) 50-48-6, 549-18-8; (paroxetine) 61869-08-7; (nefazodone) 82752-99-6, 83366-66-9; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (buspirone) 33386-08-2, 36505-84-7

L148 ANSWER 20 OF 30 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003084409 EMBASE
TITLE: The use of antidepressants in novel combination therapies.
AUTHOR: Shelton R.C.
CORPORATE SOURCE: Dr. R.C. Shelton, Vanderbilt University Medical Center, Division of Psychopharmacology, 1500 21st Ave. S., Ste. 2200, Nashville, TN 37212-8646, United States. richard.shelton@vanderbilt.edu
SOURCE: Journal of Clinical Psychiatry, (2003) 64/SUPPL. 2 (14-18). Refs: 49
ISSN: 0160-6689 CODEN: JCLPDE
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 032 Psychiatry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Antidepressant monotherapy is used more often than other therapies to achieve symptom remission in depressed patients; however, for patients resistant to antidepressants, other strategies are necessary. Many novel combination therapies have been proposed to treat resistant depression. The efficacy of combination therapies such as lithium augmentation of antidepressants is supported by a large amount of evidence including data from controlled trials. Nonetheless, anecdotal reports suggest that these combinations are underutilized. Data from studies of the use of the combination of atypical

antipsychotics and selective serotonin reuptake inhibitors suggest that this is a particularly promising therapeutic avenue. However, more research is needed to corroborate these early results.

CONTROLLED TERM: Medical Descriptors:
*depression: DR, drug resistance
*depression: DT, drug therapy
*depression: TH, therapy
drug use
combination chemotherapy
monotherapy
symptomatology
remission
drug efficacy
drug mechanism
cognitive therapy
psychotherapy
human
clinical trial
review
priority journal
Drug Descriptors:
*antidepressant agent: CT, clinical trial
*antidepressant agent: CB, drug combination
*antidepressant agent: CM, drug comparison
*antidepressant agent: DO, drug dose
*antidepressant agent: DT, drug therapy
lithium: CT, clinical trial
lithium: CB, drug combination
lithium: DT, drug therapy
atypical antipsychotic agent: CT, clinical trial
atypical antipsychotic agent: CB, drug combination
atypical antipsychotic agent: DO, drug dose
atypical antipsychotic agent: DT, drug therapy
serotonin uptake inhibitor: CT, clinical trial
serotonin uptake inhibitor: CB, drug combination
serotonin uptake inhibitor: CM, drug comparison
serotonin uptake inhibitor: DO, drug dose
serotonin uptake inhibitor: DT, drug therapy
tricyclic antidepressant agent: CT, clinical trial
tricyclic antidepressant agent: CM, drug comparison
tricyclic antidepressant agent: DT, drug therapy
noradrenalin uptake inhibitor: CB, drug combination
noradrenalin uptake inhibitor: DT, drug therapy
citalopram: CT, clinical trial
citalopram: CB, drug combination
citalopram: DT, drug therapy
thyroid hormone: CT, clinical trial
thyroid hormone: CB, drug combination
thyroid hormone: DT, drug therapy
liothyronine: CT, clinical trial
liothyronine: CB, drug combination
liothyronine: DT, drug therapy
monoamine oxidase inhibitor: CB, drug combination
monoamine oxidase inhibitor: DT, drug therapy
fluoxetine: CT, clinical trial
fluoxetine: CB, drug combination
fluoxetine: DO, drug dose
fluoxetine: DT, drug therapy
paroxetine: CT, clinical trial
paroxetine: CB, drug combination
paroxetine: DO, drug dose
paroxetine: DT, drug therapy

desipramine: CT, clinical trial
desipramine: DT, drug therapy
sertraline: CT, clinical trial
sertraline: DT, drug therapy
alprazolam: CT, clinical trial
alprazolam: DT, drug therapy
risperidone: CT, clinical trial
risperidone: CB, drug combination
risperidone: DO, drug dose
risperidone: DT, drug therapy
olanzapine: CT, clinical trial
olanzapine: CB, drug combination
olanzapine: DT, drug therapy
nortriptyline: CT, clinical trial
nortriptyline: DT, drug therapy
serotonin 2A antagonist: CB, drug combination
serotonin 2A antagonist: DT, drug therapy
serotonin 2C antagonist: CB, drug combination
serotonin 2C antagonist: DT, drug therapy
serotonin 1A agonist: CB, drug combination
serotonin 1A agonist: DT, drug therapy
buspirone: CB, drug combination
buspirone: DT, drug therapy
anticonvulsive agent: CB, drug combination
anticonvulsive agent: DT, drug therapy
carbamazepine: CB, drug combination
carbamazepine: DT, drug therapy
psychostimulant agent: CB, drug combination
psychostimulant agent: DT, drug therapy
dexamphetamine: CB, drug combination
dexamphetamine: DT, drug therapy
methylphenidate: CB, drug combination
methylphenidate: DT, drug therapy
mirtazapine: CB, drug combination
mirtazapine: DT, drug therapy
nefazodone: CB, drug combination
nefazodone: DT, drug therapy
unindexed drug
liothyronine sodium
venlafaxine

CAS REGISTRY NO.: (lithium) 7439-93-2; (citalopram) 59729-33-8; (liothyronine) 6138-47-2, 6893-02-3; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (paroxetine) 61869-08-7; (desipramine) 50-47-5, 58-28-6; (sertraline) 79617-96-2; (alprazolam) 28981-97-7; (risperidone) 106266-06-2; (olanzapine) 132539-06-1; (nortriptyline) 72-69-5, 894-71-3; (buspirone) 33386-08-2, 36505-84-7; (carbamazepine) 298-46-4, 8047-84-5; (dexamphetamine) 1462-73-3, 51-63-8, 51-64-9; (methylphenidate) 113-45-1, 298-59-9; (mirtazapine) 61337-67-5; (nefazodone) 82752-99-6, 83366-66-9; (liothyronine sodium) 55-06-1; (venlafaxine) 93413-69-5

CHEMICAL NAME: Effexor; Cytomel; Zoloft; Risperdal; Paxil; Zyprexa; Pamelor; Aventyl; Serzone; Remeron; Concerta; Ritalin; Prozac; Dextrostat; Dexedrine; Norpramin; Celexa; Carbatrol; Tegretol; Buspar; Xanax

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ACCESSION NUMBER: 2003034386 EMBASE

TITLE: Cytochrome P450 drug **interactions** within the HMG-CoA reductase inhibitor class: Are they clinically relevant?.

AUTHOR: Martin J.; Krum H.
CORPORATE SOURCE: Dr. J. Martin, Clinical Pharmacology Unit, Monash Med. School/Alfred Hospital, Commercial Rd, Prahran, Vic. 3181, Australia. jennifer.martin@med.monash.edu.au
SOURCE: Drug Safety, (2003) 26/1 (13-21).
Refs: 48
ISSN: 0114-5916 CODEN: DRSAEA
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
The present review outlines the clinical relevance of pharmacokinetic drug interactions within the HMG-CoA reductase inhibitor class. These interactions can result in markedly increased or decreased plasma concentrations of some drugs within this class. However, the relationship between altered plasma concentrations and adverse effects or toxicity may not be linear. It is likely that other variables affect this concentration-effect relationship including: rapid changes in the concentration, concomitant lipid-lowering therapy or host genetic factors that code for different forms or amounts of metabolising enzymes and drug receptors. It is not currently possible to predict which patients will manifest clinically important drug-drug interactions, nor what concentration of an HMG-CoA reductase inhibitor will cause rhabdomyolysis. Thus, until prescribers have better scientific information from which to develop a 'therapeutic range' for each agent, caution should be exercised. In particular, patients taking a CYP3A4-metabolised agent, e.g. atorvastatin, simvastatin and lovastatin, should not be started on a CYP3A4 inhibitor or inducer without close monitoring.

CONTROLLED TERM: Medical Descriptors:
*rhabdomyolysis: SI, side effect
*myopathy: SI, side effect
*myositis: SI, side effect
drug metabolism
enzyme inhibition
enzyme induction
risk assessment
drug blood level
creatine kinase blood level
drug clearance
grapefruit juice
human
review
priority journal
Drug Descriptors:
*cytochrome P450: EC, endogenous compound
*hydroxymethylglutaryl coenzyme A reductase inhibitor: AE, adverse drug reaction
*hydroxymethylglutaryl coenzyme A reductase inhibitor: CB, drug combination
***hydroxymethylglutaryl coenzyme A reductase inhibitor: IT, drug interaction**
*hydroxymethylglutaryl coenzyme A reductase inhibitor: PK, pharmacokinetics
atorvastatin: AE, adverse drug reaction
atorvastatin: CB, drug combination
atorvastatin: IT, drug interaction
atorvastatin: PK, pharmacokinetics
simvastatin: AE, adverse drug reaction
simvastatin: CB, drug combination

simvastatin: IT, drug interaction
simvastatin: PK, pharmacokinetics
mevinolin: AE, adverse drug reaction
mevinolin: CB, drug combination
mevinolin: IT, drug interaction
mevinolin: PK, pharmacokinetics
rosuvastatin: AE, adverse drug reaction
rosuvastatin: CB, drug combination
rosuvastatin: IT, drug interaction
rosuvastatin: PK, pharmacokinetics
pravastatin: AE, adverse drug reaction
pravastatin: CB, drug combination
pravastatin: IT, drug interaction
pravastatin: PK, pharmacokinetics
fluindostatin: AE, adverse drug reaction
fluindostatin: CB, drug combination
fluindostatin: IT, drug interaction
fluindostatin: PK, pharmacokinetics
cerivastatin: AE, adverse drug reaction
cerivastatin: CB, drug combination
cerivastatin: IT, drug interaction
cerivastatin: PK, pharmacokinetics
cytochrome P450 2C9: EC, endogenous compound
cytochrome P450 2C19: EC, endogenous compound
cytochrome P450 3A4: EC, endogenous compound
diltiazem: CB, drug combination
diltiazem: IT, drug interaction
itraconazole: CB, drug combination
itraconazole: IT, drug interaction
mibefradil: CB, drug combination
mibefradil: IT, drug interaction
fluoxetine: CB, drug combination
fluoxetine: IT, drug interaction
fluvoxamine: CB, drug combination
fluvoxamine: IT, drug interaction
nefazodone: CB, drug combination
nefazodone: IT, drug interaction
sertraline: CB, drug combination
sertraline: IT, drug interaction
Hypericum perforatum extract: CB, drug combination
Hypericum perforatum extract: IT, drug interaction
nelfinavir: CB, drug combination
nelfinavir: IT, drug interaction
cyclosporin: CB, drug combination
cyclosporin: IT, drug interaction
erythromycin: CB, drug combination
erythromycin: IT, drug interaction
gemfibrozil: CB, drug combination
gemfibrozil: IT, drug interaction

CAS REGISTRY NO.: (cytochrome P450) 9035-51-2; (atorvastatin) 134523-00-5, 134523-03-8; (simvastatin) 79902-63-9; (mevinolin) 75330-75-5; (rosuvastatin) 147098-18-8, 147098-20-2; (pravastatin) 81131-74-0; (fluindostatin) 93957-54-1; (cerivastatin) 143201-11-0; (cytochrome P450 3A4) 329736-03-0; (diltiazem) 33286-22-5, 42399-41-7; (itraconazole) 84625-61-6; (mibefradil) 116666-63-8; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (fluvoxamine) 54739-18-3; (nefazodone) 82752-99-6, 83366-66-9; (sertraline) 79617-96-2; (nelfinavir) 159989-64-7, 159989-65-8; (cyclosporin) 79217-60-0; (erythromycin) 114-07-8, 70536-18-4; (gemfibrozil) 25812-30-0

L148 ANSWER 22 OF 30 EMBASE
on STN

ACCESSION NUMBER: 2002016914 EMBASE
TITLE: A retrospective chart review of risperidone use in treatment-resistant children and adolescents with psychiatric disorders.
AUTHOR: Simeon J.; Milin R.; Walker S.
CORPORATE SOURCE: J. Simeon, 1145 Carling Avenue, Ottawa, Ont. K1Z 7K4, Canada
SOURCE: Progress in Neuro-Psychopharmacology and Biological Psychiatry, (2002) 26/2 (267-275).
Refs: 35
ISSN: 0278-5846 CODEN: PNPPD7
PUBLISHER IDENT.: S 0278-5846(01)00264-0
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
030 Pharmacology
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Antipsychotic drugs are used to treat a wide variety of child psychiatric disorders characterized by psychotic symptoms, aggression, excitement, tics, stereotypies and hyperactivity nonresponsive to other therapies. Unfortunately, typical antipsychotics have many adverse effects limiting their long-term use. Novel antipsychotics with combined dopaminergic and serotonergic action, such as risperidone, appear to offer better safety and efficacy profiles in controlled studies of adult patients, and therefore appeared as promising pharmacotherapeutic agents in child psychiatry. The purpose of this retrospective chart review was to obtain data on the potential effectiveness and tolerability of risperidone in children and adolescents presenting with a variety of chronic and severe psychiatric disorders who had been unresponsive to previous pharmacological treatments. Charts for 106 children and adolescents (males n=81 or 76.4%; females n=25 or 23.6%), presenting with attention deficit and/or hyperactivity disorder (n=49 or 46.2%), conduct disorder (n=13 or 12.3%), oppositional-defiant disorder (n=5 or 4.7%), behavioural problems not otherwise specified (n=2 or 1.9%), autism (n=8 or 7.5%), Asperger's syndrome (n=8 or 7.5%), pervasive developmental disorder (PDD) not otherwise specified (n=4 or 3.8%), anxiety (n=6 or 5.7%), depression (n=2 or 1.9%), dysthymia (n=2 or 1.9%), schizophrenia (n=4 or 3.8%), adjustment disorder (n=1 or 0.9%) and obsessive-compulsive disorder (n=2 or 1.9%) were reviewed retrospectively to determine the tolerability and potential efficacy of risperidone treatment for a variety of psychiatric disorders. Six subjects also presented with mental retardation. The average length of illness prior to risperidone treatment was 5 years and the average age of risperidone treatment onset was 11 years. The mean daily dose of risperidone was 1.2 mg (range=0.25 to 8.0 mg). Very few adverse effects were reported. The average length of risperidone treatment was 11 months with the majority (n=75 or 76%) of patients maintained on risperidone following study termination. Seven cases (6.6%) were missing follow-up data. The majority (n=78 or 74%) of patients were taking concurrent psychiatric medications, most commonly stimulants for the treatment of ADHD. Clinical global improvements for children and adolescents at the final study visit were marked (n=.37 or 34.9%), moderate (n=.40 or 37.7%), mild (n=13 or 12.4%), none (n=12 or 11.3%), or worse (n=1 or 1%). Three cases (2.9%) were missing clinical improvement data. Results suggest that risperidone may be useful for managing behavioural disturbances and psychotic symptoms associated with a wide variety of childhood psychiatric disorders. For most patients in the study, a combination of risperidone and adjunctive pharmacotherapy was beneficial. Controlled and discontinuation studies of risperidone treatment in children and adolescents with behavioural and psychotic disorders are recommended. .COPYRGT.

CONTROLLED TERM: Medical Descriptors:
*mental disease: DT, drug therapy
*child psychiatry
drug use
retrospective study
drug efficacy
drug tolerability
treatment failure
attention deficit disorder: DT, drug therapy
hyperactivity: DT, drug therapy
behavior disorder: DT, drug therapy
autism: DT, drug therapy
Asperger syndrome: DT, drug therapy
anxiety neurosis: DT, drug therapy
depression: DT, drug therapy
dysthymia: DT, drug therapy
schizophrenia: DT, drug therapy
mental deficiency: DT, drug therapy
obsession: DT, drug therapy
disease duration
combination chemotherapy
side effect: SI, side effect
treatment outcome
human
male
female
major clinical study
controlled study
adolescent
child
article
Drug Descriptors:
*risperidone: AE, adverse drug reaction
*risperidone: CB, drug combination
*risperidone: DO, drug dose
*risperidone: DT, drug therapy
*risperidone: PD, pharmacology
neuroleptic agent: AE, adverse drug reaction
neuroleptic agent: CB, drug combination
neuroleptic agent: DO, drug dose
neuroleptic agent: DT, drug therapy
neuroleptic agent: PD, pharmacology
dexamphetamine: CB, drug combination
dexamphetamine: DT, drug therapy
methylphenidate: CB, drug combination
methylphenidate: DT, drug therapy
pemoline: CB, drug combination
pemoline: DT, drug therapy
clomipramine: CB, drug combination
clomipramine: DT, drug therapy
imipramine: CB, drug combination
imipramine: DT, drug therapy
desipramine: CB, drug combination
desipramine: DT, drug therapy
paroxetine: CB, drug combination
paroxetine: DT, drug therapy
fluoxetine: CB, drug combination
fluoxetine: DT, drug therapy
fluvoxamine: CB, drug combination
fluvoxamine: DT, drug therapy
amfebutamone: CB, drug combination

amfebutamone: DT, drug therapy
tryptophan: CB, drug combination
tryptophan: DT, drug therapy
nefazodone: CB, drug combination
nefazodone: DT, drug therapy
trazodone: CB, drug combination
trazodone: DT, drug therapy
clonidine: CB, drug combination
clonidine: DT, drug therapy
haloperidol: CB, drug combination
haloperidol: DT, drug therapy
levomepromazine: CB, drug combination
levomepromazine: DT, drug therapy
propranolol: CB, drug combination
propranolol: DT, drug therapy
buspirone: CB, drug combination
buspirone: DT, drug therapy
lithium: CB, drug combination
lithium: DT, drug therapy
anticonvulsive agent: CB, drug combination
anticonvulsive agent: DT, drug therapy
antiparkinson agent: CB, drug combination
antiparkinson agent: DT, drug therapy

CAS REGISTRY NO.: (risperidone) 106266-06-2; (dexamphetamine) 1462-73-3, 51-63-8, 51-64-9; (methylphenidate) 113-45-1, 298-59-9; (pemoline) 2152-34-3; (clomipramine) 17321-77-6, 303-49-1; (imipramine) 113-52-0, 50-49-7; (desipramine) 50-47-5, 58-28-6; (paroxetine) 61869-08-7; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (fluvoxamine) 54739-18-3; (amfebutamone) 31677-93-7, 34911-55-2; (tryptophan) 6912-86-3, 73-22-3; (nefazodone) 82752-99-6, 83366-66-9; (trazodone) 19794-93-5, 25332-39-2; (clonidine) 4205-90-7, 4205-91-8, 57066-25-8; (haloperidol) 52-86-8; (levomepromazine) 1236-99-3, 60-99-1, 7104-38-3; (propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6; (buspirone) 33386-08-2, 36505-84-7; (lithium) 7439-93-2

L148 ANSWER 23 OF 30 EMBASE
on STN

ACCESSION NUMBER: 2002078832 EMBASE
TITLE: What role do atypical antipsychotic drugs have in treatment-resistant depression?.
AUTHOR: Thase M.E.
CORPORATE SOURCE: Dr. M.E. Thase, Western Psychiat. Inst. and Clinic, 3811 O'Hara St., Pittsburgh, PA 15213-2593, United States. thaseme@msx.upmc.edu
SOURCE: Journal of Clinical Psychiatry, (2002) 63/2 (95-103). Refs: 84
ISSN: 0160-6689 CODEN: JCLPDE
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Despite significant advances in the treatment of depression, many patients fail to respond to treatment with adequate dose and duration. Multiple therapeutic approaches are available for the treatment of patients not responding to standard antidepressant medication. These include switching medication or

combination and augmentation strategies. A substantial number of patients do not respond to multiple treatment trials. These patients suffer from treatment-resistant depression (TRD) and represent a challenge to the treating physician. There have been a growing number of reports on the use of atypical antipsychotics as augmenting agents in nonpsychotic TRD. Second-generation antipsychotics are less likely to provoke parkinsonian side effects. It has also been reported that these agents produce lower rates of tardive movement disorders than traditional neuroleptics. Furthermore, second-generation antipsychotics are serotonin-2A/2C antagonists, possibly allowing them to improve the efficacy and some aspects of the side effect profile of selective serotonin reuptake inhibitors (SSRIs). Weight gain and sedation are likely to be the most common adverse events of such combined therapy. In a recent controlled clinical trial, the atypical antipsychotic olanzapine was combined with fluoxetine therapy in an 8-week, double-blind clinical trial in patients with TRD. This combination drug therapy demonstrated clinical efficacy on several rating scales and showed rapid onset of action. Although more studies will be required to confirm and extend these findings, the results suggest that there may be a clinical benefit to combining atypical antipsychotics with SSRIs in nonpsychotic TRD.

CONTROLLED TERM: Medical Descriptors:
*therapy resistance
*depression: DR, drug resistance
*depression: DT, drug therapy
*psychosis: DR, drug resistance
*psychosis: DT, drug therapy
dose response
disease duration
parkinsonism: SI, side effect
tardive dyskinesia: SI, side effect
serotonin release
drug potentiation
drug efficacy
weight gain
sedation
rating scale
combination chemotherapy
patient compliance
motor dysfunction: SI, side effect
diarrhea: SI, side effect
nausea: SI, side effect
extrapyramidal symptom: SI, side effect
hyperprolactinemia: SI, side effect
fatigue: SI, side effect
polydipsia: SI, side effect
polyuria: SI, side effect
drowsiness: SI, side effect
sexual dysfunction: SI, side effect
sleep disorder: SI, side effect
anxiety
somnolence: SI, side effect
human
major clinical study
clinical trial
double blind procedure
article
priority journal
Drug Descriptors:
*antidepressant agent: AE, adverse drug reaction
*antidepressant agent: CB, drug combination
*antidepressant agent: DT, drug therapy
*serotonin 2A antagonist: AE, adverse drug reaction
*serotonin 2A antagonist: CB, drug combination

*serotonin 2A antagonist: DT, drug therapy
*serotonin 2C antagonist: AE, adverse drug reaction
*serotonin 2C antagonist: CB, drug combination
*serotonin 2C antagonist: DT, drug therapy
*serotonin uptake inhibitor: AE, adverse drug reaction
*serotonin uptake inhibitor: CB, drug combination
*serotonin uptake inhibitor: DT, drug therapy
*olanzapine: AE, adverse drug reaction
*olanzapine: CT, clinical trial
*olanzapine: CB, drug combination
*olanzapine: DT, drug therapy
*fluoxetine: AE, adverse drug reaction
*fluoxetine: CT, clinical trial
***fluoxetine: CB, drug combination**
*fluoxetine: DT, drug therapy
lithium: AE, adverse drug reaction
lithium: CB, drug combination
lithium: DT, drug therapy
thyroid hormone: AE, adverse drug reaction
thyroid hormone: CB, drug combination
thyroid hormone: DT, drug therapy
dopamine receptor stimulating agent: AE, adverse drug reaction
dopamine receptor stimulating agent: CB, drug combination
dopamine receptor stimulating agent: DT, drug therapy
tricyclic antidepressant agent: AE, adverse drug reaction
tricyclic antidepressant agent: CB, drug combination
tricyclic antidepressant agent: DT, drug therapy
desipramine: AE, adverse drug reaction
desipramine: CT, clinical trial
desipramine: CB, drug combination
desipramine: DT, drug therapy
buspirone: AE, adverse drug reaction
buspirone: CB, drug combination
buspirone: DT, drug therapy
pramipexole: AE, adverse drug reaction
pramipexole: CB, drug combination
pramipexole: DT, drug therapy
bromocriptine: AE, adverse drug reaction
bromocriptine: CB, drug combination
bromocriptine: DT, drug therapy
clozapine: AE, adverse drug reaction
clozapine: CB, drug combination
clozapine: DT, drug therapy
haloperidol: AE, adverse drug reaction
haloperidol: CB, drug combination
haloperidol: DT, drug therapy
serotonin: EC, endogenous compound
noradrenalin: EC, endogenous compound
dopamine: EC, endogenous compound
quetiapine: AE, adverse drug reaction
quetiapine: CB, drug combination
quetiapine: DT, drug therapy
amfebutamone: AE, adverse drug reaction
amfebutamone: CB, drug combination
amfebutamone: DT, drug therapy
chlorpromazine: AE, adverse drug reaction
chlorpromazine: CB, drug combination
chlorpromazine: DT, drug therapy
liothyronine: AE, adverse drug reaction
liothyronine: CB, drug combination
liothyronine: DT, drug therapy
nefazodone: AE, adverse drug reaction

nefazodone: CB, drug combination
nefazodone: DT, drug therapy
perphenazine: AE, adverse drug reaction
perphenazine: CB, drug combination
perphenazine: DT, drug therapy
tranylcypromine: AE, adverse drug reaction
tranylcypromine: CB, drug combination
tranylcypromine: DT, drug therapy
venlafaxine: AE, adverse drug reaction
venlafaxine: CB, drug combination
venlafaxine: DT, drug therapy
liothyronine sodium
mirtazapine
risperidone

CAS REGISTRY NO.: (olanzapine) 132539-06-1; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (lithium) 7439-93-2; (desipramine) 50-47-5, 58-28-6; (buspirone) 33386-08-2, 36505-84-7; (pramipexole) 104632-26-0; (bromocriptine) 25614-03-3; (clozapine) 5786-21-0; (haloperidol) 52-86-8; (serotonin) 50-67-9; (noradrenalin) 1407-84-7, 51-41-2; (dopamine) 51-61-6, 62-31-7; (quetiapine) 111974-72-2; (amfebutamone) 31677-93-7, 34911-55-2; (chlorpromazine) 50-53-3, 69-09-0; (liothyronine) 6138-47-2, 6893-02-3; (nefazodone) 82752-99-6, 83366-66-9; (perphenazine) 58-39-9; (tranylcypromine) 13492-01-8, 155-09-9, 54-97-7; (venlafaxine) 93413-69-5; (liothyronine sodium) 55-06-1; (mirtazapine) 61337-67-5; (risperidone) 106266-06-2

CHEMICAL NAME: Wellbutrin; Thorazine; Clozaril; Norpramin; Prozac; Haldol; Cytomel; Triostat; Remeron; Serzone; Zyprexa; Trilafon; Mirapex; Seroquel; Risperdal; Parnate; Effexor

L148 ANSWER 24 OF 30 EMBASE
on STN

ACCESSION NUMBER: 2001425487 EMBASE
TITLE: Antidepressant drug **interactions**.
AUTHOR: Botts S.R.; Alfaro C.
CORPORATE SOURCE: Prof. S.R. Botts, Univ. of Kentucky Coll. of Pharmacy, UK Mental Health Research Center, 627 West 4th Street, Lexington, KY 40508, United States. sbott2@pop.uky.edu
SOURCE: Journal of Pharmacy Practice, (2001) 14/6 (467-477).
Refs: 64
ISSN: 0897-1900 CODEN: JPPREU
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:

Second-generation antidepressants are more selective in their pharmacological mechanisms and offer fewer side effects and a safer toxicological profile than cyclic antidepressants and monoamine oxidase inhibitors. While the risk for pharmacodynamic interactions is more limited than with older agents with broader receptor effects, the risks for pharmacokinetic interactions is greater. The capacity of selective serotonin reuptake inhibitors to inhibit the metabolic activity of cytochrome P450 isozyme system has spurred over a decade of intense psychopharmacological and pharmacogenetics research to better the understanding of the significance of these interactions. Clinicians have had to increase their knowledge and understanding of drug interaction potential to better manage patients receiving these newer antidepressants. The following is a review of both pharmacodynamic and pharmacokinetic drug-drug interactions

with antidepressants.

CONTROLLED TERM: Medical Descriptors:
*depression: DT, drug therapy
*psychopharmacology
drug metabolism
drug induced disease: SI, side effect
pharmacodynamics
pharmacogenetics
drug receptor binding
drug conjugation
drug blood level
amino acid sequence
drug clearance
toxicity: SI, side effect
human
review
Drug Descriptors:
*antidepressant agent: AE, adverse drug reaction
*antidepressant agent: CR, drug concentration
***antidepressant agent: IT, drug interaction**
*antidepressant agent: DT, drug therapy
cytochrome P450: EC, endogenous compound
monoamine oxidase inhibitor: AE, adverse drug reaction
monoamine oxidase inhibitor: CB, drug combination
monoamine oxidase inhibitor: DO, drug dose
monoamine oxidase inhibitor: IT, drug interaction
monoamine oxidase inhibitor: DT, drug therapy
monoamine oxidase inhibitor: PK, pharmacokinetics
monoamine oxidase inhibitor: PD, pharmacology
serotonin uptake inhibitor: AE, adverse drug reaction
serotonin uptake inhibitor: CB, drug combination
serotonin uptake inhibitor: DO, drug dose
serotonin uptake inhibitor: IT, drug interaction
serotonin uptake inhibitor: DT, drug therapy
serotonin uptake inhibitor: PK, pharmacokinetics
serotonin uptake inhibitor: PD, pharmacology
citalopram: AE, adverse drug reaction
citalopram: CB, drug combination
citalopram: CR, drug concentration
citalopram: DO, drug dose
citalopram: IT, drug interaction
citalopram: DT, drug therapy
metoprolol: CB, drug combination
metoprolol: IT, drug interaction
fluoxetine: CB, drug combination
fluoxetine: DO, drug dose
fluoxetine: IT, drug interaction
fluoxetine: DT, drug therapy
fluoxetine: PK, pharmacokinetics
fluoxetine: PD, pharmacology
alprazolam: CB, drug combination
alprazolam: CR, drug concentration
alprazolam: IT, drug interaction
alprazolam: DT, drug therapy
clonazepam: CB, drug combination
clonazepam: IT, drug interaction
clonazepam: DT, drug therapy
fluvoxamine: CB, drug combination
fluvoxamine: IT, drug interaction
fluvoxamine: DT, drug therapy
fluvoxamine: PK, pharmacokinetics
fluvoxamine: PD, pharmacology

carbamazepine: CM, drug comparison
carbamazepine: IT, drug interaction
calcium channel blocking agent: CB, drug combination
calcium channel blocking agent: IT, drug interaction
calcium channel blocking agent: PD, pharmacology
cisapride: CB, drug combination
cisapride: IT, drug interaction
antihistaminic agent: CB, drug combination
antihistaminic agent: DT, drug therapy
clozapine: CB, drug combination
clozapine: IT, drug interaction
propranolol: CB, drug combination
propranolol: CR, drug concentration
propranolol: IT, drug interaction
diazepam: CB, drug combination
diazepam: CR, drug concentration
diazepam: IT, drug interaction
paroxetine: CB, drug combination
paroxetine: IT, drug interaction
paroxetine: PK, pharmacokinetics
neuroleptic agent: CB, drug combination
neuroleptic agent: IT, drug interaction
sertraline: CB, drug combination
sertraline: CR, drug concentration
sertraline: DO, drug dose
sertraline: DT, drug therapy
sertraline: PK, pharmacokinetics
sertraline: PD, pharmacology
venlafaxine: CB, drug combination
venlafaxine: IT, drug interaction
venlafaxine: DT, drug therapy
venlafaxine: PD, pharmacology
nefazodone: AE, adverse drug reaction
nefazodone: CB, drug combination
nefazodone: IT, drug interaction
nefazodone: DT, drug therapy
nefazodone: PK, pharmacokinetics
nefazodone: PD, pharmacology
hydroxymethylglutaryl coenzyme A reductase inhibitor: AE, adverse drug reaction
hydroxymethylglutaryl coenzyme A reductase inhibitor: CB, drug combination
hydroxymethylglutaryl coenzyme A reductase inhibitor: IT, drug interaction
hydroxymethylglutaryl coenzyme A reductase inhibitor: PD, pharmacology
amfebutamone: CB, drug combination
amfebutamone: IT, drug interaction
amfebutamone: DT, drug therapy
amfebutamone: PK, pharmacokinetics
amfebutamone: PD, pharmacology
proteinase inhibitor: CB, drug combination
proteinase inhibitor: IT, drug interaction
proteinase inhibitor: PD, pharmacology
mirtazapine: CB, drug combination
mirtazapine: IT, drug interaction
mirtazapine: DT, drug therapy
mirtazapine: PK, pharmacokinetics
mirtazapine: PD, pharmacology
reboxetine: CB, drug combination
reboxetine: IT, drug interaction
reboxetine: DT, drug therapy

reboxetine: PK, pharmacokinetics
reboxetine: PD, pharmacology
Hypericum perforatum extract: CB, drug combination
Hypericum perforatum extract: IT, drug interaction
Hypericum perforatum extract: DT, drug therapy
Hypericum perforatum extract: PK, pharmacokinetics
Hypericum perforatum extract: PD, pharmacology
oral contraceptive agent: CB, drug combination
oral contraceptive agent: IT, drug interaction
oral contraceptive agent: PO, oral drug administration
unindexed drug

CAS REGISTRY NO.: (cytochrome P450) 9035-51-2; (citalopram) 59729-33-8; (metoprolol) 37350-58-6; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (alprazolam) 28981-97-7; (clonazepam) 1622-61-3; (fluvoxamine) 54739-18-3; (carbamazepine) 298-46-4, 8047-84-5; (cisapride) 81098-60-4; (clozapine) 5786-21-0; (propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6; (diazepam) 439-14-5; (paroxetine) 61869-08-7; (sertraline) 79617-96-2; (venlafaxine) 93413-69-5; (nefazodone) 82752-99-6, 83366-66-9; (amfebutamone) 31677-93-7, 34911-55-2; (proteinase inhibitor) 37205-61-1; (mirtazapine) 61337-67-5; (reboxetine) 98769-81-4

L148 ANSWER 25 OF 30 EMBASE
on STN

ACCESSION NUMBER: 2001129545 EMBASE
TITLE: Loss of response to antidepressants and subsequent refractoriness: Diagnostic issues in a retrospective case series.
AUTHOR: Sharma V.
CORPORATE SOURCE: V. Sharma, Mood Disorders Unit, London Psychiatric Hospital, 850 Highbury Avenue, London, Ont., Canada. vsharma@julian.uwo.ca
SOURCE: Journal of Affective Disorders, (2001) 64/1 (99-106).
Refs: 41
ISSN: 0165-0327 CODEN: JADID7
PUBLISHER IDENT.: S 0165-0327(00)00212-3
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
032 Psychiatry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:

Background: The loss of response to antidepressant drugs is not an uncommon phenomenon. While some patients respond to changes in the drug regimen, others develop resistance to various treatment modalities. Method: I describe 15 cases who had a loss of response to repeated trials of antidepressants before developing a chronic and severe, refractory depression. Results: These patients had failed to respond to various treatment strategies including substitution with other antidepressant drugs, augmentation with agents such as T3 and lithium; and finally electroconvulsive therapy (ECT). Following discontinuation of antidepressants and treatment with mood stabilizers, there was a sustained improvement. Notably some of the patients who had earlier failed to respond to mood stabilizers in combination with unimodal antidepressants improved upon discontinuation of antidepressants and continued treatment with mood stabilizers. Limitations: Open trial, retrospective design and small sample size. Conclusion: These clinical findings suggest that some refractory depressives represent cryptic bipolar disorders. Prospective validation is necessary to support this conclusion. .COPYRGT. 2001 Elsevier Science B.V.

CONTROLLED TERM: Medical Descriptors:
*depression: DR, drug resistance
*depression: DT, drug therapy
*depression: TH, therapy
*manic depressive psychosis: DR, drug resistance
*manic depressive psychosis: DT, drug therapy
*manic depressive psychosis: TH, therapy
*psychopharmacotherapy
retrospective study
treatment outcome
mood
long term care
clinical feature
combination chemotherapy
drug withdrawal
electroconvulsive therapy
add on therapy
drug efficacy
human
male
female
clinical article
controlled study
aged
adult
article
priority journal
Drug Descriptors:
*antidepressant agent: CB, drug combination
*antidepressant agent: DT, drug therapy
liothyronine: CB, drug combination
liothyronine: DT, drug therapy
lithium: CB, drug combination
lithium: DT, drug therapy
tranquilizer: CB, drug combination
tranquilizer: DT, drug therapy
imipramine: CB, drug combination
imipramine: DT, drug therapy
phenelzine: CB, drug combination
phenelzine: DT, drug therapy
fluoxetine: CB, drug combination
fluoxetine: DT, drug therapy
valproate semisodium: CB, drug combination
valproate semisodium: DT, drug therapy
chlorpromazine: CB, drug combination
chlorpromazine: DT, drug therapy
olanzapine: CB, drug combination
olanzapine: DT, drug therapy
venlafaxine: CB, drug combination
venlafaxine: DT, drug therapy
nefazodone: CB, drug combination
nefazodone: DT, drug therapy
sertraline: CB, drug combination
sertraline: DT, drug therapy
paroxetine: CB, drug combination
paroxetine: DT, drug therapy
moclobemide: CB, drug combination
moclobemide: DT, drug therapy
carbamazepine: CB, drug combination
carbamazepine: DT, drug therapy
risperidone: CB, drug combination
risperidone: DT, drug therapy
clonazepam: CB, drug combination

clonazepam: DT, drug therapy
trimipramine: CB, drug combination
trimipramine: DT, drug therapy
lithium carbonate: CB, drug combination
lithium carbonate: DT, drug therapy
levomepromazine: CB, drug combination
levomepromazine: DT, drug therapy
zopiclone: CB, drug combination
zopiclone: DT, drug therapy
amitriptyline: CB, drug combination
amitriptyline: DT, drug therapy
amoxapine: CB, drug combination
amoxapine: DT, drug therapy
amfebutamone: CB, drug combination
amfebutamone: DT, drug therapy
benzodiazepine derivative: CB, drug combination
benzodiazepine derivative: DT, drug therapy
clomipramine: CB, drug combination
clomipramine: DT, drug therapy
dexamphetamine: CB, drug combination
dexamphetamine: DT, drug therapy
diazepam: CB, drug combination
diazepam: DT, drug therapy
unindexed drug

CAS REGISTRY NO.: (liothyronine) 6138-47-2, 6893-02-3; (lithium) 7439-93-2; (imipramine) 113-52-0, 50-49-7; (phenelzine) 156-51-4, 51-71-8; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (valproate semisodium) 76584-70-8; (chlorpromazine) 50-53-3, 69-09-0; (olanzapine) 132539-06-1; (venlafaxine) 93413-69-5; (nefazodone) 82752-99-6, 83366-66-9; (sertraline) 79617-96-2; (paroxetine) 61869-08-7; (moclobemide) 71320-77-9; (carbamazepine) 298-46-4, 8047-84-5; (risperidone) 106266-06-2; (clonazepam) 1622-61-3; (trimipramine) 25332-13-2, 739-71-9; (lithium carbonate) 554-13-2; (levomepromazine) 1236-99-3, 60-99-1, 7104-38-3; (zopiclone) 43200-80-2; (amitriptyline) 50-48-6, 549-18-8; (amoxapine) 14028-44-5; (amfebutamone) 31677-93-7, 34911-55-2; (clomipramine) 17321-77-6, 303-49-1; (dexamphetamine) 1462-73-3, 51-63-8, 51-64-9; (diazepam) 439-14-5

L148 ANSWER 26 OF 30 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2000084121 EMBASE
TITLE: New approaches to the treatment of **refractory** depression.
AUTHOR: Fava M.
CORPORATE SOURCE: Dr. M. Fava, Depression Clinical/Research Program, Massachusetts General Hospital, WACC 815, 15 Parkman St., Boston, MA 02114, United States. mfava@partners.org
SOURCE: Journal of Clinical Psychiatry, (2000) 61/SUPPL. 1 (26-32). Refs: 75
ISSN: 0160-6689 CODEN: JCLPDE
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Although the majority of patients with depression respond well to their initial pharmacologic treatment, as many as 30% to 45% fail to achieve an adequate

response. In addition to the more traditional lithium and thyroid hormone augmentation strategies, a number of new pharmacotherapeutic approaches are currently being used to help manage refractory depression, including the addition of another agent or a switch to another antidepressant. Augmentation and switching strategies are often selected in order to obtain a different neurochemical effect (e.g., adding a relatively noradrenergic agent to a relatively serotonergic antidepressant). In particular, several studies have suggested that depressed patients refractory to treatment with selective serotonin reuptake inhibitors (SSRIs) may show a good response to newer agents that have a pharmacologic profile distinct from the SSRIs. Furthermore, preliminary studies have shown that the addition of SSRIs to either noradrenergic drugs such as the tricyclic antidepressants (TCAs) or dopaminergic agents may be efficacious, even though concerns about drug-drug interactions and tricyclic cardiac toxicity have limited the use of TCA-SSRI combinations. The introduction of reboxetine, a relatively selective norepinephrine reuptake inhibitor, may increase the use of the latter therapeutic approach because of its improved safety profile compared with the TCAs. The review of treatment options for refractory depression that follows will outline the advantages, disadvantages, and level of support for a number of new treatment strategies.

CONTROLLED TERM: Medical Descriptors:
*depression: DT, drug therapy
treatment failure
hormone substitution
drug safety
drug efficacy
drug tolerability
cardiotoxicity: SI, side effect
serotonin syndrome: SI, side effect
tremor: SI, side effect
panic: SI, side effect
hypertension: SI, side effect
sedation
weight gain
human
clinical trial
review
priority journal
Drug Descriptors:
*serotonin uptake inhibitor: AE, adverse drug reaction
*serotonin uptake inhibitor: CT, clinical trial
*serotonin uptake inhibitor: CB, drug combination
***serotonin uptake inhibitor: IT, drug interaction**
*serotonin uptake inhibitor: DT, drug therapy
*tricyclic antidepressant agent: AE, adverse drug reaction
*tricyclic antidepressant agent: CT, clinical trial
*tricyclic antidepressant agent: CB, drug combination
***tricyclic antidepressant agent: IT, drug interaction**
*tricyclic antidepressant agent: DT, drug therapy
*noradrenalin uptake inhibitor: DT, drug therapy
*reboxetine: DT, drug therapy
thyroid hormone: CT, clinical trial
lithium: CT, clinical trial
lithium: DT, drug therapy
dopamine receptor stimulating agent: CT, clinical trial
dopamine receptor stimulating agent: CB, drug combination
dopamine receptor stimulating agent: DT, drug therapy
buspirone: AE, adverse drug reaction
buspirone: CT, clinical trial
buspirone: CB, drug combination
buspirone: DT, drug therapy

pindolol: CB, drug combination
pindolol: DT, drug therapy
nefazodone: AE, adverse drug reaction
nefazodone: CT, clinical trial
nefazodone: CB, drug combination
nefazodone: DT, drug therapy
amfebutamone: AE, adverse drug reaction
amfebutamone: CT, clinical trial
amfebutamone: CB, drug combination
amfebutamone: DT, drug therapy
venlafaxine: AE, adverse drug reaction
venlafaxine: CT, clinical trial
venlafaxine: CB, drug combination
venlafaxine: DT, drug therapy
mirtazapine: AE, adverse drug reaction
mirtazapine: CT, clinical trial
mirtazapine: CB, drug combination
mirtazapine: DT, drug therapy
desipramine: AE, adverse drug reaction
desipramine: CT, clinical trial
desipramine: CB, drug combination
desipramine: DT, drug therapy
anticonvulsive agent: CB, drug combination
anticonvulsive agent: DT, drug therapy
neuroleptic agent: CT, clinical trial
neuroleptic agent: CB, drug combination
neuroleptic agent: DT, drug therapy
monoamine oxidase inhibitor: AE, adverse drug reaction
monoamine oxidase inhibitor: CT, clinical trial
monoamine oxidase inhibitor: CB, drug combination
monoamine oxidase inhibitor: IT, drug interaction
monoamine oxidase inhibitor: DT, drug therapy
psychostimulant agent: AE, adverse drug reaction
psychostimulant agent: CT, clinical trial
psychostimulant agent: CB, drug combination
psychostimulant agent: IT, drug interaction
psychostimulant agent: DT, drug therapy
amantadine: CT, clinical trial
amantadine: CB, drug combination
amantadine: DT, drug therapy
citalopram: AE, adverse drug reaction
citalopram: CT, clinical trial
citalopram: CB, drug combination
citalopram: IT, drug interaction
citalopram: DT, drug therapy
carbamazepine
dexamphetamine
valproate semisodium
fluoxetine: AE, adverse drug reaction
fluoxetine: CT, clinical trial
fluoxetine: CB, drug combination
fluoxetine: IT, drug interaction
fluoxetine: DT, drug therapy
fluvoxamine
gabapentin
lamotrigine
levothyroxine: CT, clinical trial
methylphenidate
olanzapine
unindexed drug
fluvoxamine maleate
levothyroxine sodium
pemoline magnesium

pergolide mesilate
pramipexole
vestra
risperidone
sertraline
liothyronine sodium

CAS REGISTRY NO.: (reboxetine) 98769-81-4; (lithium) 7439-93-2; (buspirone) 33386-08-2, 36505-84-7; (pindolol) 13523-86-9, 21870-06-4; (nefazodone) 82752-99-6, 83366-66-9; (amfebutamone) 31677-93-7, 34911-55-2; (venlafaxine) 93413-69-5; (mirtazapine) 61337-67-5; (desipramine) 50-47-5, 58-28-6; (amantadine) 665-66-7, 768-94-5; (citalopram) 59729-33-8; (carbamazepine) 298-46-4, 8047-84-5; (dexamphetamine) 1462-73-3, 51-63-8, 51-64-9; (valproate semisodium) 76584-70-8; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (fluvoxamine) 54739-18-3; (gabapentin) 60142-96-3; (lamotrigine) 84057-84-1; (levothyroxine) 51-48-9; (methylphenidate) 113-45-1, 298-59-9; (olanzapine) 132539-06-1; (fluvoxamine maleate) 61718-82-9; (levothyroxine sodium) 55-03-8; (pemoline magnesium) 18968-99-5; (pergolide mesilate) 66104-23-2; (pramipexole) 104632-26-0; (risperidone) 106266-06-2; (sertraline) 79617-96-2; (liothyronine sodium) 55-06-1

CHEMICAL NAME: Symmetrel; Wellbutrin; Buspar; Tegretol; Celexa; Norpramin; Dexedrine; Depakote; Prozac; Luvox; Neurontin; Lamictal; Synthroid; Ritalin; Remeron; Serzone; Zyprexa; Cylert; Permax; Mirapex; Vestra; Risperdal; Zoloft; Cytomel; Effexor

L148 ANSWER 27 OF 30 EMBASE
on STN

ACCESSION NUMBER: 2000295889 EMBASE

TITLE: Pharmacokinetic and pharmacodynamic consequences of metabolism-based drug **interactions** with alprazolam, midazolam, and triazolam.

AUTHOR: Yuan R.; Flockhart D.A.; Balian J.D.

CORPORATE SOURCE: Dr. R. Yuan, HFD-860, CDER-OPS-OCPB-DPE I, Woodmont-II building, 5600 Fishers Lane, Rockville, MD 20857, United States

SOURCE: Journal of Clinical Pharmacology, (1999) 39/11 (1109-1125). Refs: 93
ISSN: 0091-2700 CODEN: JCPCBR

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 030 Pharmacology
032 Psychiatry
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:
This review was conducted to identify the current data on drug interactions with alprazolam, midazolam, and triazolam to guide practitioners in the use of these drugs. The Medline electronic database from 1966 through 1998 was used to identify clinical studies of the pharmacokinetic effect of drugs on these three benzodiazepines. Of a total of 491 literature reports identified, 59 prospective studies met our selection criteria. The pharmacokinetic parameters of AUC, C(max), t(1/2), and t(max) were evaluated for changes following an interaction. To allow comparison between studies, changes in the parameters were normalized relative to the control values. Pharmacodynamic effects and measures, when reported in the original studies as statistically significant, were classified as a strong interaction, and when the interaction was present but not statistically significant, they were classified as mild in this review. As a result, clinically significant drug interactions were noted for all three

benzodiazepines, although iris clear that statistically significant pharmacokinetic changes do not always translate into clinically significant pharmacodynamic consequences. All three benzodiazepines were susceptible to drug interactions, but oral dosing of midazolam and triazolam resulted in greater alterations in the pharmacokinetic parameters than alprazolam due to their larger presystemic extraction. Ketoconazole and itraconazole were found to be the most potent metabolic inhibitors that prolonged the duration of or intensified the magnitude of the dynamic response produced by the three benzodiazepines. Rifampin, carbamazepine, and phenytoin were noted to be potent metabolic inducers, and their treatments result in loss of benzodiazepine therapeutic efficacy. In conclusion, potent metabolic inhibitors and inducers can either significantly prolong or diminish the dynamic effects of benzodiazepines via their influence on the pharmacokinetics of benzodiazepines.

CONTROLLED TERM: Medical Descriptors:
*drug metabolism
pharmacodynamics
drug half life
area under the curve
anxiety neurosis: DT, drug therapy
mental disease: DT, drug therapy
food drug interaction
drug bioavailability
human
major clinical study
clinical trial
randomized controlled trial
double blind procedure
crossover procedure
controlled study
review
Drug Descriptors:
*alprazolam: CT, clinical trial
*alprazolam: AD, drug administration
*alprazolam: CB, drug combination
*alprazolam: CM, drug comparison
*alprazolam: CR, drug concentration
*alprazolam: DO, drug dose
***alprazolam: IT, drug interaction**
*alprazolam: DT, drug therapy
*alprazolam: PK, pharmacokinetics
*alprazolam: PO, oral drug administration
*midazolam: CT, clinical trial
*midazolam: AD, drug administration
*midazolam: CB, drug combination
*midazolam: CM, drug comparison
*midazolam: CR, drug concentration
*midazolam: DO, drug dose
***midazolam: IT, drug interaction**
*midazolam: DT, drug therapy
*midazolam: PK, pharmacokinetics
*midazolam: PO, oral drug administration
*triazolam: CT, clinical trial
*triazolam: AD, drug administration
*triazolam: CB, drug combination
*triazolam: CM, drug comparison
*triazolam: CR, drug concentration
*triazolam: DO, drug dose
***triazolam: IT, drug interaction**
*triazolam: DT, drug therapy
*triazolam: PK, pharmacokinetics
*triazolam: PO, oral drug administration

*hypnotic sedative agent: CT, clinical trial
*hypnotic sedative agent: AD, drug administration
*hypnotic sedative agent: CB, drug combination
*hypnotic sedative agent: CM, drug comparison
*hypnotic sedative agent: CR, drug concentration
*hypnotic sedative agent: DO, drug dose
***hypnotic sedative agent: IT, drug interaction**
*hypnotic sedative agent: DT, drug therapy
*hypnotic sedative agent: PK, pharmacokinetics
*hypnotic sedative agent: PO, oral drug administration
ketoconazole: CT, clinical trial
ketoconazole: CB, drug combination
ketoconazole: DO, drug dose
ketoconazole: IT, drug interaction
ketoconazole: PO, oral drug administration
itraconazole: CT, clinical trial
itraconazole: CB, drug combination
itraconazole: DO, drug dose
itraconazole: IT, drug interaction
itraconazole: PO, oral drug administration
nefazodone: CT, clinical trial
nefazodone: CB, drug combination
nefazodone: DO, drug dose
nefazodone: IT, drug interaction
nefazodone: PO, oral drug administration
erythromycin: CT, clinical trial
erythromycin: CB, drug combination
erythromycin: DO, drug dose
erythromycin: IT, drug interaction
erythromycin: IV, intravenous drug administration
erythromycin: PO, oral drug administration
fluoxetine: CT, clinical trial
fluoxetine: CB, drug combination
fluoxetine: DO, drug dose
fluoxetine: IT, drug interaction
fluvoxamine: CT, clinical trial
fluvoxamine: CB, drug combination
fluvoxamine: DO, drug dose
fluvoxamine: IT, drug interaction
cimetidine: CT, clinical trial
cimetidine: CB, drug combination
cimetidine: DO, drug dose
cimetidine: IT, drug interaction
dextropropoxyphene: CT, clinical trial
dextropropoxyphene: CB, drug combination
dextropropoxyphene: DO, drug dose
dextropropoxyphene: IT, drug interaction
oral contraceptive agent: CT, clinical trial
oral contraceptive agent: AD, drug administration
oral contraceptive agent: CB, drug combination
oral contraceptive agent: DO, drug dose
oral contraceptive agent: IT, drug interaction
oral contraceptive agent: PO, oral drug administration
ethinylestradiol: CT, clinical trial
ethinylestradiol: AD, drug administration
ethinylestradiol: CB, drug combination
ethinylestradiol: DO, drug dose
ethinylestradiol: IT, drug interaction
ethinylestradiol: PO, oral drug administration
carbamazepine: CT, clinical trial
carbamazepine: CB, drug combination
carbamazepine: DO, drug dose
carbamazepine: IT, drug interaction

carbamazepine: PO, oral drug administration
ritonavir: CT, clinical trial
ritonavir: CB, drug combination
ritonavir: DO, drug dose
ritonavir: IT, drug interaction
clarithromycin: CT, clinical trial
clarithromycin: CB, drug combination
clarithromycin: DO, drug dose
clarithromycin: IT, drug interaction
clarithromycin: PO, oral drug administration
antibiotic agent: CT, clinical trial
antibiotic agent: CB, drug combination
antibiotic agent: DO, drug dose
antibiotic agent: IT, drug interaction
antibiotic agent: IV, intravenous drug administration
antibiotic agent: PO, oral drug administration
antivirus agent: CT, clinical trial
antivirus agent: CB, drug combination
antivirus agent: DO, drug dose
antivirus agent: IT, drug interaction
diltiazem: CT, clinical trial
diltiazem: CB, drug combination
diltiazem: DO, drug dose
diltiazem: IT, drug interaction
diltiazem: PO, oral drug administration
verapamil: CT, clinical trial
verapamil: CB, drug combination
verapamil: DO, drug dose
verapamil: IT, drug interaction
verapamil: PO, oral drug administration
calcium channel blocking agent: CT, clinical trial
calcium channel blocking agent: CB, drug combination
calcium channel blocking agent: DO, drug dose
calcium channel blocking agent: IT, drug interaction
calcium channel blocking agent: PO, oral drug administration
ranitidine: CT, clinical trial
ranitidine: CB, drug combination
ranitidine: DO, drug dose
ranitidine: IT, drug interaction
ranitidine: PO, oral drug administration
histamine H2 receptor antagonist: CT, clinical trial
histamine H2 receptor antagonist: CB, drug combination
histamine H2 receptor antagonist: DO, drug dose
histamine H2 receptor antagonist: IT, drug interaction
histamine H2 receptor antagonist: PO, oral drug administration
rifampicin: CT, clinical trial
rifampicin: CB, drug combination
rifampicin: DO, drug dose
rifampicin: IT, drug interaction
phenytoin: CT, clinical trial
phenytoin: CB, drug combination
phenytoin: DO, drug dose
phenytoin: IT, drug interaction
phenytoin: PO, oral drug administration
anticonvulsive agent: CT, clinical trial
anticonvulsive agent: CB, drug combination
anticonvulsive agent: DO, drug dose
anticonvulsive agent: IT, drug interaction
anticonvulsive agent: PO, oral drug administration

placebo
antifungal agent: CT, clinical trial
antifungal agent: CB, drug combination
antifungal agent: DO, drug dose
antifungal agent: IT, drug interaction
antifungal agent: PO, oral drug administration
unindexed drug

CAS REGISTRY NO.: (alprazolam) 28981-97-7; (midazolam) 59467-70-8; (triazolam) 28911-01-5; (ketoconazole) 65277-42-1; (itraconazole) 84625-61-6; (nefazodone) 82752-99-6, 83366-66-9; (erythromycin) 114-07-8, 70536-18-4; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (fluvoxamine) 54739-18-3; (cimetidine) 51481-61-9, 70059-30-2; (dextropropoxyphene) 1639-60-7, 469-62-5; (ethinylestradiol) 57-63-6; (carbamazepine) 298-46-4, 8047-84-5; (ritonavir) 155213-67-5; (clarithromycin) 81103-11-9; (diltiazem) 33286-22-5, 42399-41-7; (verapamil) 152-11-4, 52-53-9; (ranitidine) 66357-35-5, 66357-59-3; (rifampicin) 13292-46-1; (phenytoin) 57-41-0, 630-93-3

L148 ANSWER 28 OF 30 EMBASE
on STN

ACCESSION NUMBER: 1998317791 EMBASE
TITLE: Serotonergic **synergism**: The risks and benefits of combining the selective serotonin reuptake inhibitors with other serotonergic drugs.
AUTHOR: DeBattista C.; Sofuoglu M.; Schatzberg A.F.
CORPORATE SOURCE: Dr. C. DeBattista, Dept. of Psychiatry/Behavioral Sci., Stanford Univ. School of Medicine, Stanford, CA 94305-5723, United States
SOURCE: Biological Psychiatry, (1998) 44/5 (341-347).
Refs: 76
ISSN: 0006-3223 CODEN: BIPCBF
PUBLISHER IDENT.: S 0006-3223(98)00161-9
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:

It has become common clinical practice to combine the selective serotonin reuptake inhibitors with other serotonergic agents for augmentation or adjunctive purposes. The empirical basis for using these combinations remains limited, but is growing. Also growing is a literature that suggests that even the most apparently benign combinations of serotonergic drugs carry at least some risk of serious pharmacokinetic or pharmacodynamic drug interactions, such as a serotonin syndrome.

CONTROLLED TERM: Medical Descriptors:
*depression: DT, drug therapy
*serotonin syndrome: SI, side effect
hyponatremia: SI, side effect
sexual dysfunction: DT, drug therapy
sexual dysfunction: SI, side effect
seizure: SI, side effect
insomnia: DT, drug therapy
migraine: DT, drug therapy
irritability
nausea: SI, side effect
vomiting: SI, side effect
akathisia: DT, drug therapy

akathisia: SI, side effect
drug safety
drug potentiation
drug mixture
human
clinical trial
randomized controlled trial
double blind procedure
crossover procedure
controlled study
oral drug administration
article
priority journal
Drug Descriptors:
*serotonin uptake inhibitor: AE, adverse drug reaction
*serotonin uptake inhibitor: CB, drug combination
***serotonin uptake inhibitor: IT, drug interaction**
*serotonin 1a agonist: CB, drug combination
***serotonin 1a agonist: IT, drug interaction**
*serotonin 1a antagonist: CB, drug combination
***serotonin 1a antagonist: IT, drug interaction**
*serotonin 1d receptor
histamine h2 receptor antagonist: CB, drug combination
histamine h2 receptor antagonist: IT, drug interaction
beta adrenergic receptor blocking agent: CB, drug combination
beta adrenergic receptor blocking agent: IT, drug interaction
monoamine oxidase inhibitor: AE, adverse drug reaction
monoamine oxidase inhibitor: CB, drug combination
monoamine oxidase inhibitor: IT, drug interaction
serotonin 3 antagonist: AE, adverse drug reaction
serotonin 3 antagonist: CB, drug combination
serotonin 3 antagonist: IT, drug interaction
serotonin 3 antagonist: DT, drug therapy
cisapride: AE, adverse drug reaction
cisapride: CB, drug combination
cisapride: IT, drug interaction
cisapride: DT, drug therapy
ondansetron: AE, adverse drug reaction
ondansetron: CB, drug combination
ondansetron: IT, drug interaction
ondansetron: DT, drug therapy
lithium: AE, adverse drug reaction
lithium: CB, drug combination
lithium: IT, drug interaction
fenfluramine: CB, drug combination
fenfluramine: IT, drug interaction
dexfenfluramine: CB, drug combination
dexfenfluramine: IT, drug interaction
cyproheptadine: CB, drug combination
cyproheptadine: IT, drug interaction
cyproheptadine: DT, drug therapy
pindolol: AE, adverse drug reaction
pindolol: CT, clinical trial
pindolol: CB, drug combination
pindolol: DO, drug dose
pindolol: IT, drug interaction
propranolol: AE, adverse drug reaction
propranolol: CT, clinical trial
propranolol: CB, drug combination
propranolol: DO, drug dose

propranolol: IT, drug interaction
propranolol: DT, drug therapy
buspirone: AE, adverse drug reaction
buspirone: CT, clinical trial
buspirone: CB, drug combination
buspirone: DO, drug dose
buspirone: IT, drug interaction
paroxetine: CT, clinical trial
paroxetine: CB, drug combination
paroxetine: DO, drug dose
paroxetine: IT, drug interaction
sertraline: CT, clinical trial
sertraline: CB, drug combination
sertraline: DO, drug dose
sertraline: IT, drug interaction
fluoxetine: AE, adverse drug reaction
fluoxetine: CT, clinical trial
fluoxetine: CB, drug combination
fluoxetine: DO, drug dose
fluoxetine: IT, drug interaction
fluoxetine: DT, drug therapy
tranylcypromine: CB, drug combination
tranylcypromine: IT, drug interaction
trazodone: CB, drug combination
trazodone: IT, drug interaction
trazodone: DT, drug therapy
nefazodone: AE, adverse drug reaction
nefazodone: CB, drug combination
nefazodone: IT, drug interaction
fluvoxamine: CT, clinical trial
fluvoxamine: CB, drug combination
fluvoxamine: IT, drug interaction
sumatriptan: AE, adverse drug reaction
sumatriptan: AD, drug administration
sumatriptan: CB, drug combination
sumatriptan: IT, drug interaction
sumatriptan: DT, drug therapy
amfebutamone: CT, clinical trial
amfebutamone: CB, drug combination
amfebutamone: IT, drug interaction
amfebutamone: DT, drug therapy
olanzapine: AE, adverse drug reaction
olanzapine: CB, drug combination
olanzapine: IT, drug interaction
clozapine: AE, adverse drug reaction
clozapine: CB, drug combination
clozapine: IT, drug interaction
moclobemide: AE, adverse drug reaction
moclobemide: CB, drug combination
moclobemide: IT, drug interaction
unindexed drug

CAS REGISTRY NO.: (cisapride) 81098-60-4; (ondansetron) 103639-04-9, 116002-70-1, 99614-01-4; (lithium) 7439-93-2; (fenfluramine) 404-82-0, 458-24-2; (dexfenfluramine) 3239-44-9, 3239-45-0; (cyproheptadine) 129-03-3, 969-33-5; (pindolol) 13523-86-9, 21870-06-4; (propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6; (buspirone) 33386-08-2, 36505-84-7; (paroxetine) 61869-08-7; (sertraline) 79617-96-2; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (tranylcypromine) 13492-01-8, 155-09-9, 54-97-7; (trazodone) 19794-93-5, 25332-39-2; (nefazodone) 82752-99-6, 83366-66-9; (fluvoxamine) 54739-18-3; (sumatriptan) 103628-46-2;

(amfebutamone) 31677-93-7, 34911-55-2; (olanzapine) 132539-06-1; (clozapine) 5786-21-0; (moclobemide) 71320-77-9

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ACCESSION NUMBER: 97179871 EMBASE
DOCUMENT NUMBER: 1997179871
TITLE: **Dangerous** interaction with nefazodone added to fluoxetine, desipramine, venlafaxine, valproate and clonazepam combination therapy [2].
AUTHOR: Benazzi F.
CORPORATE SOURCE: F. Benazzi, Department of Psychiatry, Public Hospital 'Morgagni', 47100 Forli, Italy. f.benazzi@fo.nettuno.it
SOURCE: Journal of Psychopharmacology, (1997) 11/2 (190-191).
Refs: 11
ISSN: 0269-8811 CODEN: JOPSEQ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 008 Neurology and Neurosurgery
029 Clinical Biochemistry
030 Pharmacology
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:
*muscle weakness: SI, side effect
*paresthesia: SI, side effect
adult
case report
depression: DT, drug therapy
drug clearance
drug half life
drug mechanism
female
female sexual dysfunction: SI, side effect
human
letter
panic: DT, drug therapy
priority journal
xerostomia: SI, side effect
Drug Descriptors:
***antidepressant agent: IT, drug interaction**
*antidepressant agent: CB, drug combination
*antidepressant agent: AE, adverse drug reaction
*antidepressant agent: DT, drug therapy
*antidepressant agent: PD, pharmacology
*clonazepam: PD, pharmacology
*clonazepam: DT, drug therapy
***clonazepam: IT, drug interaction**
*clonazepam: CB, drug combination
*clonazepam: AE, adverse drug reaction
*desipramine: CB, drug combination
*desipramine: AE, adverse drug reaction
*desipramine: DT, drug therapy
*desipramine: PK, pharmacokinetics
*desipramine: PD, pharmacology
***desipramine: IT, drug interaction**
*fluoxetine: DT, drug therapy
*fluoxetine: AE, adverse drug reaction
*fluoxetine: PK, pharmacokinetics

*fluoxetine: PD, pharmacology
***fluoxetine: IT, drug interaction**
***fluoxetine: CB, drug combination**
***nefazodone: CB, drug combination**
*nefazodone: PD, pharmacology
*nefazodone: DT, drug therapy
***nefazodone: IT, drug interaction**
*nefazodone: AE, adverse drug reaction
*valproic acid: PD, pharmacology
*valproic acid: AE, adverse drug reaction
*valproic acid: CB, drug combination
***valproic acid: IT, drug interaction**
*valproic acid: DT, drug therapy
***venlafaxine: IT, drug interaction**
*venlafaxine: DT, drug therapy
*venlafaxine: CB, drug combination
*venlafaxine: AE, adverse drug reaction
serotonin 1a antagonist: PD, pharmacology
serotonin 1a antagonist: DT, drug therapy
serotonin 1a antagonist: IT, drug interaction
serotonin 1a antagonist: CB, drug combination
serotonin 1a antagonist: AE, adverse drug reaction
serotonin 1a receptor: EC, endogenous compound

CAS REGISTRY NO.: (clonazepam) 1622-61-3; (desipramine) 50-47-5, 58-28-6; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (nefazodone) 82752-99-6, 83366-66-9; (valproic acid) 1069-66-5, 99-66-1; (venlafaxine) 93413-69-5

L148 ANSWER 30 OF 30 EMBASE
on STN

ACCESSION NUMBER: 97305526 EMBASE
DOCUMENT NUMBER: 1997305526
TITLE: Retrospective study of selegiline-antidepressant drug **interactions** and a review of the literature.
AUTHOR: Ritter J.L.; Alexander B.
CORPORATE SOURCE: J.L. Ritter, Univ of Washington Med Ctr-Roosevelt, 4245 Roosevelt Way N.E., Seattle, WA 98105-6920, United States
SOURCE: Annals of Clinical Psychiatry, (1997) 9/1 (7-13).
Refs: 37
ISSN: 1040-1237 CODEN: APSYEZ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
008 Neurology and Neurosurgery
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:

Selegiline is a selective monoamine oxidase inhibitor used in the treatment of Parkinson's disease. It is estimated that approximately one-half of Parkinsonian patients will develop depression requiring antidepressant drug treatment. Recently, selegiline's package insert was revised to reflect the potential risk of adverse effects when it is used in combination with selective serotonin reuptake inhibitors and tricyclic antidepressants. The objective of our study is to assess the safety of combining selegiline with antidepressants. A retrospective chart review was performed on all 28 patients with Parkinson's disease receiving selegiline and antidepressants concurrently to identify possible drug interactions. Compliance was assessed according to prescription refill records. Suspected adverse reactions with combination therapy were documented. There was a total of 40 selegiline-antidepressant drug combinations involving tricyclic antidepressants (n = 25), selective serotonin reuptake

inhibitors (n = 7), trazodone (n = 5), and bupropion (n = 3). One patient receiving fluoxetine developed a reaction consistent with the serotonin syndrome; however, it was never documented as such. No other selegiline drug interactions were found. Adverse effects noted were typical of antidepressant monotherapy. Although no selegiline drug interactions were documented in our study, the concurrent administration of selegiline and selective serotonin reuptake inhibitors should be avoided because of literature-reported interactions. We believe that bupropion, tricyclic antidepressants, and trazodone are reasonable choices in combination with selegiline, although tricyclic antidepressants and trazodone may be reserved as second-line treatments.

CONTROLLED TERM: Medical Descriptors:
*depression: DT, drug therapy
*depression: ET, etiology
*parkinson disease: DT, drug therapy
*parkinson disease: ET, etiology
adult
aged
amnesia: SI, side effect
anxiety neurosis: SI, side effect
article
brain hemorrhage: SI, side effect
concentration loss: SI, side effect
confusion: SI, side effect
constipation: SI, side effect
dementia: SI, side effect
dream
drowsiness: SI, side effect
drug contraindication
drug fatality: SI, side effect
falling
fatigue: SI, side effect
hallucination: SI, side effect
human
hyperpyrexia: SI, side effect
insomnia: SI, side effect
major clinical study
male
nausea: SI, side effect
nervousness
orthostatic hypotension: SI, side effect
patient compliance
priority journal
restlessness: SI, side effect
retrospective study
seizure: SI, side effect
serotonin syndrome: SI, side effect
tremor: SI, side effect
vertigo: SI, side effect
vomiting: SI, side effect
xerostomia: SI, side effect
side effect
Drug Descriptors:
*antidepressant agent: CB, drug combination
*antidepressant agent: DT, drug therapy
*antidepressant agent: DO, drug dose
*selegiline: CB, drug combination
*selegiline: AE, adverse drug reaction
*selegiline: DT, drug therapy
***selegiline: IT, drug interaction**
amfebutamone: DT, drug therapy
amfebutamone: IT, drug interaction

amfebutamone: DO, drug dose
amfebutamone: CB, drug combination
amfebutamone: AE, adverse drug reaction
amitriptyline: DO, drug dose
amitriptyline: AE, adverse drug reaction
amitriptyline: IT, drug interaction
amitriptyline: CB, drug combination
amitriptyline: DT, drug therapy
amoxapine: CB, drug combination
amoxapine: DO, drug dose
amoxapine: DT, drug therapy
carbidopa plus levodopa: AE, adverse drug reaction
carbidopa plus levodopa: CB, drug combination
carbidopa plus levodopa: IT, drug interaction
carbidopa plus levodopa: DT, drug therapy
clomipramine: DO, drug dose
clomipramine: DT, drug therapy
clomipramine: CB, drug combination
desipramine: CB, drug combination
desipramine: DO, drug dose
desipramine: IT, drug interaction
desipramine: DT, drug therapy
doxepin: CB, drug combination
doxepin: DO, drug dose
doxepin: DT, drug therapy
fluoxetine: DT, drug therapy
fluoxetine: IT, drug interaction
fluoxetine: CB, drug combination
fluoxetine: AE, adverse drug reaction
fluvoxamine maleate: CM, drug comparison
fluvoxamine maleate: DO, drug dose
fluvoxamine maleate: DT, drug therapy
imipramine: CB, drug combination
imipramine: DO, drug dose
imipramine: DT, drug therapy
imipramine: IT, drug interaction
isocarboxazid: DT, drug therapy
isocarboxazid: IT, drug interaction
isocarboxazid: CB, drug combination
maprotiline: CB, drug combination
maprotiline: DO, drug dose
maprotiline: DT, drug therapy
monoamine oxidase inhibitor: IT, drug interaction
monoamine oxidase inhibitor: AE, adverse drug reaction
monoamine oxidase inhibitor: DT, drug therapy
monoamine oxidase inhibitor: CB, drug combination
nefazodone: DO, drug dose
nefazodone: CB, drug combination
nefazodone: DT, drug therapy
nefazodone: IT, drug interaction
nortriptyline: CB, drug combination
nortriptyline: DO, drug dose
nortriptyline: DT, drug therapy
nortriptyline: IT, drug interaction
paroxetine: CB, drug combination
paroxetine: DO, drug dose
paroxetine: DT, drug therapy
phenelzine: DT, drug therapy
phenelzine: IT, drug interaction
phenelzine: CB, drug combination
protriptyline: DT, drug therapy
protriptyline: CB, drug combination
protriptyline: DO, drug dose

serotonin uptake inhibitor: AE, adverse drug reaction
serotonin uptake inhibitor: DT, drug therapy
serotonin uptake inhibitor: IT, drug interaction
serotonin uptake inhibitor: DO, drug dose
serotonin uptake inhibitor: CB, drug combination
sertraline: DO, drug dose
sertraline: CB, drug combination
sertraline: DT, drug therapy
sertraline: IT, drug interaction
tranylcypromine: DT, drug therapy
tranylcypromine: IT, drug interaction
tranylcypromine: CB, drug combination
trazodone: CB, drug combination
trazodone: IT, drug interaction
trazodone: DT, drug therapy
tricyclic antidepressant agent: IT, drug interaction
tricyclic antidepressant agent: DT, drug therapy
tricyclic antidepressant agent: CB, drug combination
tricyclic antidepressant agent: AE, adverse drug reaction
trimipramine: DT, drug therapy
trimipramine: DO, drug dose
trimipramine: CB, drug combination
venlafaxine: CB, drug combination
venlafaxine: DO, drug dose
venlafaxine: IT, drug interaction
venlafaxine: DT, drug therapy

CAS REGISTRY NO.: (selegiline) 14611-51-9, 14611-52-0, 2079-54-1, 2323-36-6; (amfebutamone) 31677-93-7, 34911-55-2; (amitriptyline) 50-48-6, 549-18-8; (amoxapine) 14028-44-5; (carbidopa plus levodopa) 57308-51-7; (clomipramine) 17321-77-6, 303-49-1; (desipramine) 50-47-5, 58-28-6; (doxepin) 1229-29-4, 1668-19-5; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (fluvoxamine maleate) 61718-82-9; (imipramine) 113-52-0, 50-49-7; (isocarboxazid) 59-63-2; (maprotiline) 10262-69-8, 10347-81-6; (nefazodone) 82752-99-6, 83366-66-9; (nortriptyline) 72-69-5, 894-71-3; (paroxetine) 61869-08-7; (phenelzine) 156-51-4, 51-71-8; (protriptyline) 1225-55-4, 438-60-8; (sertraline) 79617-96-2; (tranylcypromine) 13492-01-8, 155-09-9, 54-97-7; (trazodone) 19794-93-5, 25332-39-2; (trimipramine) 25332-13-2, 739-71-9; (venlafaxine) 93413-69-5

CHEMICAL NAME: Sinemet; Elavil; Endep; Anafranil; Norpramin; Adapin; Sinequan; Tofranil; Pamelor; Vivactil; Surmontil; Prozac; Paxil; Luvox; Nardil; Parnate; Marplan; Desyrel; Wellbutrin; Asendin; Ludiomil; Effexor; Serzone

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